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Vol. V. Fasc. 6 15 : XII 1926 N:o 28

Stockholm: P. A. Norstedt & Söner

New York: Paul B. Hoeber Inc., 76 Fifth Avenue

ACTA RADIOLOGICA

Editor: Professor Gösta Forssell, M. D., Stockholm, Sweden

Subscriptions and communications should be addressed to the Editorial Secretary of Acta Radiologica, c/o P. A. Norstedt & Söner, Stockholm, Sweden

Subscriptions and advertisements from America may be sent to Mr Paul B. Hoeber, 76 Fifth Avenue, New York Cy.

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ACTA RADIOLOGICA, published by *the Societies for Medical Radiology* in *Denmark, Finland, Holland, Norway, Sweden* and *Switzerland,* contain articles pertaining to *roentgenology, radium therapy, light therapy and electrotherapy.* These articles are published in English, French or German according to the decision of the author. Each volume comprises about 500 pages, distributed in six occasional numbers. *Subscriptions* may be forwarded to the Editorial Secretary, c/o P. A. Norstedt & Söner, Stockholm, Sweden. Subscriptions and advertisements from *America* may be sent to *Mr Paul B. Hoeber, 76 Fifth Avenue, New York Cy.*

Subscription to Vol. V: *in England 32 s. or 25 sw. crowns. in U. S. A. $ 7.*

ACTA RADIOLOGICA, herausgegeben von den *Gesellschaften für medizinische Radiologie* in *Dänemark, Finnland, Holland, Norwegen, Schweden* und in der *Schweiz,* enthalten Arbeiten auf den Gebieten der *Röntgenologie, Radiumtherapie, Lichttherapie* und *Elektrotherapie.* Die Beiträge werden je nach eigener Wahl des Verfassers, in deutscher, englischer oder französischer Sprache veröffentlicht. Jeder Band enthält c:a 500 Seiten, in sechs zwangfreien Heften erscheinend. *Abonnement* bei der Redaktion, p. a. Herren P. A. Norstedt & Söner, Stockholm, Schweden. **Abonnementspreis** für Band V: *25 schw. Kronen.*

ACTA RADIOLOGICA, revue publiée par les *sociétés pour radiologie médicale du Danemark, de la Finlande, de la Hollande, de la Norvège, de la Suède* et *de la Suisse,* contient des ouvrages dans les domaines de la *roentgenologie,* de la *radiumthérapie,* de *l'héliothérapie* et de *l'électricité médicale.* Les études sont publiées en français, anglais ou allemand au choix de l'auteur. Chaque volume renferme environ 500 pages et est distribué en six fascicules, qui paraitront dès que seront imprimés les articles à y être insérés. *On s'abonne chez* le bureau de rédaction, chez Messieurs P. A. Norstedt & Söner, Stockholm, Suède. **Prix de l'abonnement** du Volume V: *en France et en Italie 70 francs français ou 25 couronnes suéd. En Scandinavie, en Hollande et dans tous les autres pays: 25 couronnes suéd.*

För utförande av engelska översättningar rekommenderas Dr Carl Westman (leg. läkare, England), Karlaplan 8, Stockholm. Tel. Ö. 50 39.

ACTA RADIOLOGICA

EDITA PER SOCIETATES RADIOLOGICAS DANIÆ, FENNIÆ, HELVETIÆ, HOLLANDIÆ, NORVEGIÆ ET SUECIÆ

VOL. V FASC. 6 15:XII 1926 N:o 28

PRIMARY CHONDROMA OF THE LUNG[1]

A Roentgenological and Pathological Study Based upon an Analysis of Forty Cases, with a Report of Two New Cases

by

Preston M. Hickey and *Walter M. Simpson*

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(Tabulæ XXXV—XXXIX)

As the border line of advancement in the field of lung surgery goes steadily forward, the demand upon the roentgenologist for the accurate differentiation of various lung lesions becomes more urgent. It is with this fact in mind that the writers have undertaken to report two cases of pulmonary chondroma, and to analyze the data obtained from previously reported cases, in an endeavor to establish certain pertinent diagnostic criteria which might prove of value in identifying these tumors *intra vitam*. This subject should be of particular interest to the roentgenologist because the shadows produced by these tumors have never yet been correctly interpreted, if one is to judge from the information gleaned from the available literature on the subject.

It is of more than passing significance to note that the greatest interest in pulmonary chondromata was manifested in the middle-half of last century, when cellular pathology was coming into its own, and when new and added emphasis was being placed upon anatomical diagnoses. This period was followed by a quarter of a century during which interest in lung chondromata appears to have waned, certainly not because of decreased incidence, but probably because of the feeling that such growths were invariably accidental discoveries at the necropsy table, and, hence, quite devoid of clinical

[1] From the Pathological Laboratory and from the Department of Roentgenology, Medical School, University of Michigan, U. S. A.

interest. To prove that such a belief is unjustified in the light of our present-day knowledge is one of the purposes of this paper. In the past few years, thanks to progress in the field of roentgenology, interest in these tumors has been revived.

A study of the available literature discloses but thirty-eight previous reports of human cases,[1] and of these but seven have been written in English. But one important contribution appears in American medical literature — that of McGLUMPHY (27), who reports four cases. Most pathological text-books dismiss the matter with a single statement as to the rarity of such tumors. The fact that over one-half of the cases have been reported since 1900 would tend to indicate that these tumors are much more common than is generally believed. Many instances have been reported of the occurrence of primary chondromas in the lungs of lower animals. KITT described a large nodular chondro-adenoma which projected from the right main bronchus in the lung of a horse. PEACH (41) told of an encapsulated, nodulated enchondromatous tumor, $2^1/_2$ by 3 inches, in the lung of an ass. GURLT, FŒRSTER, BRUCKMÜLLER, PEUCH, and WILLIGK have described pulmonary chondromas in cattle, while NOCARD and CADÉAC have reported similar tumors in dogs (42). Two cases have been encountered in the Pathological Laboratory of the University of Michigan Hospital within the past five years.

The first of these two cases will be briefly dealt with since there was no roentgenological examination of the thorax.

Case one

Mr. J. G., aged 62. *Clinical diagnosis:* Cancer of the stomach.

Pathological diagnosis: Autopsy A-31-X. Prosector, Dr. A. S. WARTHIN. Primary adenocarcinoma of the stomach. Recent laparotomy; pylorectomy. Old syphilis. Fibroid heart. Aortic and coronary atherosclerosis. Chronic fibroid pancreatitis. General arteriosclerosis. Atrophy and chronic passive congestion of all organs. Chronic adhesive pleuritis. Myxofibro lipo adenochondroma of lung. Chronic obliterative appendicitis. Chronic prostatitis.

Gross description of lung tumor. In the anterior portion of the lower lobe of the right lung, situated just beneath the pleura, is a firm, spherical mass, measuring 12 mm. by 16 mm. It is definitely encapsulated, of cartilaginous consistence, and separated easily from the surrounding lung tissue. The surface presents small nodular irregularities. The tumor is not connected with any of the larger bronchi.

Microscopically, (Figs. 1, 2 and 3) the tumor is found to be made up largely of irregular cartilage islands, with considerable calcification of the hyaline ground substance. On a single cross-section the cartilage islands

[1] Tabulated abstracts of previously reported cases appear at the end of this paper.

number about twenty. These are surrounded by a relatively acellular perichondrium. In the septa between the cartilage units may be seen considerable myxomatous connective tissue, mature fibrous connective tissue, adipose tissue and peculiar branching, papilliferous gland-like structures, covered by a single layer of cubical or columnar epithelial cells, devoid of cilia. In one area, the papilliferous ingrowths into the lumen simulate somewhat the appearance seen in intracanalicular myxadenofibromata of the breast. At one extremity of the tumor, the cartilage islands are covered in part by stratified ciliated columnar epithelium. At one point, a transition from the stratified ciliated epithelium to the non-ciliated simple layer can be traced. The surrounding lung tissue shows the effect of pressure, but is otherwise entirely normal.

Case two

History. Mr. J. S., a 58 year old factory worker, a native of Holland, was admitted to the hospital January 27, 1926. His complaint at the time of entrance was pain in the upper left abdominal quadrant. This pain had been present for about two months. The patient came to the United States twelve years ago. His previous history is uneventful. He was married and had three children, living and well.

Physical examination showed a poorly nourished adult male lying quietly in bed. Mental state was clear. The examination of the chest showed the heart to be somewhat enlarged. On percussion, the lungs showed increased resonance. Auscultation revealed emphysematous respiration. There was marked spasm of the left rectus muscle. The spleen was not palpable. The liver was enlarged. The Wassermann was negative. Hemoglobin, 70 %; red blood cells, 5,000,000; white blood cells, 9,000; eosinophiles, 2 %.

X-Ray examination of the gastro-intestinal tract showed no evidence of pyloric obstruction. There was no evidence of any defect in the outline of the stomach suggestive of gastric neoplasm. There was a definite ileostasis seen both at twenty-four and forty-eight hours. Gastro-intestinal examination was negative for evidence of cancer of the stomach, but did suggest partial obstruction of the lower ileum.

In the preliminary fluoroscopic examination of the chest there was noted a round shadow about the size of a lemon in the right lung field. This rounded shadow was distinct from the hilum and apparently not associated with it. The mass moved with respiration.

A further study of the shadow in the right lung field was made by taking stereoscopic x-ray films in the postero-anterior position (Fig. 4). The mass was seen to be somewhat rounded in outline and apparently homogeneous in its periphery. In the centre were found small discrete areas of increased density suggestive of calcification. Both in the lateral fluoroscopic examination and in the stereoscopic films it was apparent that the rounded mass was about two fingers' breadth from the anterior chest wall. There was no evidence of fluid in either pleural cavity. The rounded mass in the right lung field was unique, there being no other shadow found in the lung field of similar appearance. In the differential diagnosis, the possibility of carcinoma was considered but excluded on account of the sharp contour. Sarcoma was excluded because of the fact that the shadow was definitely discrete and unique. With the exception of the small areas of increased density in the

center, the shadows seemed quite homogeneous. This fact favored a diagnosis of capsulated fluid with central calcification. Interlobar pleurisy was excluded on account of the definite circular appearance. Of the different types of cysts which were considered an echinococcus cyst seemed to be the most plausible. However, this would not account for the central calcified areas.

The patient was given a barium enema, which demonstrated a very large cecum, which was definitely fixed and tender. The patient was in considerable distress and an exploratory laparotomy was finally decided upon. On opening the abdomen, the gall bladder was found to be very large, extending down into the pelvis. The wall was much thickened and reddened. The gall-bladder contained about one and a half pints of fluid. There were distinct carcinomatous nodules in the liver. No growth was found in the stomach. There was no common duct obstruction. The dependent two-thirds of the gall-bladder was amputated.

The patient rallied from the operation but gradually became weaker and died twelve days after the operation.

Pathological diagnosis: Autopsy A-165-AD. Prosectors: Dr. C. V. WELLER and Dr. W. M. SIMPSON. Adenocarcinoma scirrhosum of prostate gland, with metastases in lung, liver, mesenteric and retroperitoneal lymph nodes. Carcinomatous infiltration of cystic and common bile ducts, head of pancreas and other retroperitoneal tissues. Laparotomy; partial cholecystectomy. Localized subacute fibrinopurulent peritonitis. Phlegmonous gastritis. Subacute purulent bronchitis and early broncho-pneumonia. Icterus. Chronic catarrhal cholecystitis. Chronic atrophic catarrhal gastritis. Acute exacerbation of a chronic passive congestion of all organs. Edema of lungs. Left-sided hydrothorax. Myxo-fibro-lipo-osteo-adeno-chondroma of lung. Chronic adhesive pleuritis. Agonal bacterial embolism.

Gross description of lung tumor. In the antero-inferior portion of the upper lobe of the right lung at a point 2 cm. beneath the pleura is an extremely hard, spherical tumor, 5 cm. in diameter (Fig. 6). Its surface presents multiple nodular irregularities, and is of a mottled yellowish-white color. A firm connective tissue capsule surrounds the tumor. The tumor separates from most of the surrounding tissue when section is attempted. Cross-section is made with difficulty, the knife meeting grating resistance. The cut surface presents many grayish, translucent islands of cartilaginous consistence. These appear to be surrounded in some places by whitish, stony-hard, irregular areas, rich in lime-salts and of bony consistence. Very vascular, reddish-brown, irregular areas are seen on one side of the tumor. Between the cartilaginous and calcified islands are connective tissue septa and patches of yellowish, fat-like tissue. The tumor does not appear to have any intimate association with the bronchi.

Microscopical description. Cartilage islands, varying in size from one mm. to a cm. in diameter, dominate the microscopical picture. The cartilage masses possess a rich hyaline matrix, quite uniformly homogeneous for the most part, but, showing here and there small patches of fibrocartilage. Cartilaginous bridges occasionally connect adjacent islands. The cartilage cells are usually gathered together in groups of 4 to 12 in the larger islands, while they appear to be more uniformly scattered through the smaller units, the latter being much more cellular than the large islands. Much of the cartilage contains irregular lime-salt deposits, most marked towards the center of the cartilage masses. Towards the center of a few of the larger islands,

necrosis of the cartilage has occurred, in part liquefaction and in part caseous. In the caseous areas, many cholesterol clefts are seen.

In only a few small areas has actual osseous transformation occurred (Fig. 7). In these regions, a fatty and vascular bone marrow is seen between the cancellous bone trabeculae.

In the septa between the chondromatous units is abundant loose vascular connective-tissue, some of which is of the embryonic, mucous connective tissue type. Clumps of fat tissue cells are seen in the connective tissue at intervals.

Irregular, branching, somewhat papilliferous, epithelial-lined lumina are present in the loose tissue of the septa (Fig. 8). These are lined by simple cuboidal and columnar epithelium. At no point do these epithelial cells show any transition to the respiratory epithelium of the surrounding lung tissue. In the connective tissue are areas of diffuse lymphocyte infiltration. A relatively thin connective tissue capsule separates the tumor structures from the neighboring lung parenchyma. The lung just outside the capsule shows only the changes seen in brown induration (chronic passive congestion).

Gross Characteristics

To the naked eye, pulmonary chrondromas are usually round or oval and vary considerably in size. The average size is about that of a walnut, although many attain orange size. In FOERSTER's (14) case, the cartilaginous tumors were of bean size, while those described by BUSSE (6), LINSER (26) and SCHUMANN (35) nearly completely filled one side of the thoracic cavity. The consistence of these tumors is, of course, hard and frequently rock-like.

Two macroscopic characteristics of these tumors which are of particular importance from the standpoint of roentgen-ray diagnosis are the invariable nodular, lobulated structure and the tendency for these tumors to undergo calcification or osseous transformation. The nodular appearance is produced by conglomeration of cartilaginous units, separated by septa of connective tissue. As regards the multiplicity of individual cartilage islands, chondromas of the lung show the same characteristics as those which arise so frequently at the skeletal articulations, particularly at the phalangeal joints. The lobular structure is seen not only at the periphery, but on section, yellowish-white, or grayish, translucent, opalescent irregular islands of cartilage are usually seen to be separated by vascularized connective tissue or adipose tissue. The surface lobules vary in size in proportion to the size of the cartilage units. Some have been described as of millet-seed size while others assume the size of a pea or cherry.

The tumor is usually surrounded by a firm connective tissue capsule, which shows no derivation from the surrounding lung tissue.

In most cases, the encapsulated tumor has separated very readily from the neighboring lung parenchyma. In a few instances, the capsule of subpleural chondromata was connected with the adjacent lung tissue only by means of a slender pedicle.

On section of the tumor, the knife usually grates because of lime-salt deposits. In the grayish or bluish translucent cartilage units may be seen chalk-white plaques. The whitish areas may be due merely to lime-salt impregnation of the hyaline cartilage or they may represent true ossification, with bone-marrow development. In many cases the tumors were described as possessing a firm cartilaginous periphery and a rock-like, calcareous or osseous central portion. More often, however, the calcified or osseous areas are distributed in an irregular, patchy fashion. In the osseous portions may sometimes be seen reddish-brown areas of bone-marrow, with cancellous bony trabeculae.

The connective tissue septa which separate the cartilaginous units are usually quite vascular and not infrequently show a gelatinous, myxomatous degeneration. One surprising feature of these tumors is the relative abundance of adipose tissue which may be found between and apparently extending into the cartilage islands. In many cases, the fat tissue was easily distinguished in the gross. In FELLER's (13) case, the tumor macroscopically simulated a lipoma.

In the tissue between the agglomerated cartilage nodules may sometimes be seen cyst-like spaces, filled with albuminous or mucinous fluid. The significance of these is usually not revealed until microscopic examination is done.

Microscopical Characteristics

There is a striking similarity in most of the microscopical descriptions. Cartilage is the most prominent element. It is usually of the hyaline type, although a few have described areas of fibrocartilage or cartilage with many elastic fibers. As seen in the gross, the cartilage is usually found in islands, with occasional cartilaginous bridges connecting adjacent units. A distinct perichondrium surrounds the cartilage masses. The arrangement of the cartilage cells varies markedly. One writer (31) described their distribution as being similar to that seen in the epiphyses, but for the most part the cells appear to be clumped in small, irregular, atypical groups, with considerable hyaline ground substance intervening.

The cartilage masses towards the center of the tumor frequently show some evidence of retrogressive metamorphosis. In some, this

takes the form of myxedematous degeneration or liquefaction necrosis. In the majority, calcification occurred. The calcium granules may be fine and uniformly distributed through the hyaline matrix or the granules may be coarse and be gathered principally about the clumps of cartilage cells, with non-calcified ground-substance between the groups of cells.

True bone formation was described by five writers, and two of the tumors showed areas of bone-marrow. Osteoid tissue was described by two writers.

The connective tissue of the capsule and interlobular septa may be quite vascular. In two cases, there were large, irregular blood spaces. Frequently, much of the connective tissue is of the myxomatous, embryonic variety.

More or less adipose tissue was described in more than one-half of the cases. It is usually intermixed with the connective tissue or it alone completely fills the interval between the cartilage islands. Two authors described small areas of smooth muscle between the cartilage masses.

Perhaps the most interesting discovery on histological examination is the finding of peculiar epithelial-lined spaces, in the interlobular clefts, most often appearing as elongated lumina, lined by parallel rows of cuboidal or columnar cells — usually the former. The epithelial cells are non-ciliated in practically every case. Two observers describe small areas of ciliated cylindrical cells. In a few instances the gland-like lumina become dilated, to form cystic spaces, filled with richly albuminous fluid or mucinous secretion. One looks in vain for any evidence of gradual transition of the epithelium lining these irregular spaces into the respiratory epithelium of the neighboring lung alveoli. Not infrequently the alveolar-like arrangement of the cuboidal cells suggests the appearance of the regenerating alveolar epithelium (so-called cells of Tripier) seen particularly in chronic fibroid pneumonia and in chronic fibrocaseous pulmonary tuberculosis. In some cases, the myxomatous connective tissue immediately adjacent to the cubical epithelium produces intracanalicular projections, simulating somewhat the picture seen in the intracanalicular myxadenofibromas of the breast. In one case, that of TAPIE (37), the epithelial cells apparently underwent malignant transformation.

It is at once evident, then, that the components of these tumors constitute a bronchial complex, with representatives of all of the histological elements which go to make up mature bronchi.

Anatomical Location

The location of these tumors is exceedingly variable. The majority, at least twenty-six, were in close proximity to the pleura. SCHULTZ (34), BUSSE (6), and REISSIG (32) considered their tumors to be pleural in origin. VIGOUROUX and HÉRISSON-LAPARRE (38), as well as BLEU (4), described pedunculated tumors in the pleural cavity with the pedicles attached to the pleura. Twenty writers emphasized that the tumors encountered by them were either covered in part by the pleura or were separated from it by a few millimeters of healthy lung tissue. Nearly every one of these writers has insisted that the tumor had no connection with the bronchi. In six cases only, two of CHIARI's (8 and 9) and those of CAUSSADE, SURMONT and LACAPÈRE (7), FELLER (13), ADAMSON (3), and SIEGERT (36), did the tumor appear to have any close association with the bronchial cartilages. LEBERT (23) described his tumor as occurring between the pulmonary lobes. Four of the tumors were situated near the root of the lung, but none was connected with a bronchus. In no case did the tumor appear to originate in the mediastinum and extend secondarily into the lung parenchyma. There seems to be no predilection for either lung. The variability in the location of these tumors, as well as their usual peripheral location and their lack of contact with the bronchi, offer interesting material for a discussion as to their probable origin.

Histogenesis

Certainly most of these tumors cannot be classed as simple ecchondroses. Their complexity and failure of intimate association with the bronchi argues against any such possibility. Some writers have intimated that these tumors may have originated from the bronchial cartilages and that they secondarily became separated, thus ultimately appearing as isolated neoplasms. The frequent pleural and subpleural situation tends to exclude such a genesis.

HART (15) is of the opinion that the location of many of these tumors in situations where no legitimate cartilage anlagen should be present, and the very complexity of their components, gives conclusive evidence of their true neoplastic character. Because of the admixture of connective tissue derivatives and epithelial structures, he classed them with the teratomas. If one defines a teratoma as a tumor having origin in a developmental disturbance — one which is out of time, place, and degree embryologically, then such a de-

signation seems quite correct. HART called his tumor an »adeno-fibro-lipo-chondroma myxomatosum».

CHIARI was the first to give to these tumors a name which described their complex structure. He termed them »lipo-chondro-adenomas».

MCGLUMPHY (27) considered that the tumors described by him were unique in medical literature and to these chondromas with epithelial elements he gave the name »adenochondroma». CHIARI, HART, ABRIKOSOFF (1), KITT, and SCHMIDT, had already applied this term to similar new growths described previously.

In the two cases of CHIARI, the tumors were found in bronchiectatic cavities, which led CHIARI to assume that such tumors represented hyperplastic growths from the bronchi as the result of chronic inflammation. Such a theory receives no support from the other writers on this topic. In FELLER's case, the tumor was apparently intrabronchial, but there was no evidence of inflammation. In SIEGERT's case, the bronchial lumen was almost completely filled by the tumor, but evidence of inflammatory stimulus to growth was lacking. In the case reported by CAUSSADE, SURMONT and LACAPÈRE, a pedunculated tumor in the right primary bronchus almost completely obliterated the lumen and had caused an obstructive type of purulent bronchitis and bullous emphysema of the right lung. But in this case the inflammatory condition was unquestionably a sequel and not a precedent. Furthermore, any theory which attempts to attach an inflammatory etiology to the tumors of this type found elsewhere in the lung must fail because by far the majority of writers have emphasized the fact that the neighboring lung tissue showed no pathological changes.

FELLER points out that the components of these tumors are all structural elements of lung tissue, and he compares these tumors structurally to adenofibromas of the breast. Using ALBRECHT's terminology (43), he calls these mixed lung tumors »hamartomas», meaning that they are tumor-like growths resulting from the faulty mixture of the normal components of an organ. It is true that many of the tumors embrace all of the bronchial anlagen — both mesodermal (cartilage, fat tissue, connective tissue, smooth muscle, etc.) and entodermal (epithelial) structures.

It seems quite reasonable to explain the genesis of these tumors as the result of the perverse development of bronchial anlagen. They must have their origin, then, very early in fetal development. BORST (5) found a walnut-size chondroma, in a case of pronounced anthracosis, with complete absence of carbon pigment in the tumor, which led him to assume that the tumor developed very early in life. No

writer has described anthracosis in these lung tumors, although many have described abundant carbon pigment elsewhere in the nearby lung tissue.

The pulmonary chondromata probably have little in common genetically with the more complex »dermoid cysts» and trigerminal teratomas which are found with relative frequency in the mediastinum and rarely in the lungs. Cartilage and bone may be found in such structures. Of 39 cases of »dermoid cysts» and teratoma of the anterior mediastinum collected by CHRISTIAN (44), 4 ultimately became embedded largely in lung tissue, although the mediastinal origin could still be traced. All but 2 of CHRISTIAN's 39 cases were simple bigerminal dermoid cysts, with ectodermal (skin) and some mesodermal derivatives. CHRISTIAN believed that many of these were primarily of branchiogenic origin, secondarily displaced into the mediastinum during the descent of the heart, great vessels, thyroid gland and thymus. Another explanation of these mediastinal dermoid growths is that they represent germ tissue displaced at the time of closure of the anterior chest wall. The more complex trigerminal teratomata (embryomata) are probably best explained by the »isolated blastomere» theory, with the lung teratoma representing an imperfectly developed, included twin fetus.

Certainly, a study of the anatomical locations of the pulmonary chondromata dismisses at once any possibility that the tumors which form the subject of this thesis originate primarily in the mediastinum.

In summary, then, it might be said that the so-called pulmonary chondromas probably represent tumors having origin in aberrant bronchial anlagen, since all of the structures which go to make up these mixed tumors are normal components of the bronchi.

Diagnosis

In accurate roentgenological interpretation lies the hope for the proper diagnosis of these neoplasms during life. Physical signs have been of no value in differentiating the few larger tumors from other intrathoracic disease, and in almost every instance careful percussion and auscultation gave no evidence of tumor.

The sharply circumscribed character of the pulmonary chondromas serves to distinguish them from those conditions which are of an inflammatory genesis. The sharply-defined periphery of the chondromas is almost invariably surrounded by healthy, air-containing lung parenchyma. This absence of irregular peripheral inflammatory

infiltrations serves to distinguish this condition from old tuberculous lesions with calcification or old abscesses with calcification. Likewise, the peculiar branching bone formations (pneumopathia osteoplastica racemosa) which have been occasionally described should present no problem in differential diagnosis. Most of these cases of arborescent bone formation have occurred in the emphysematous lungs of old persons, and usually show no relation to bronchi or vessels. LUSCHKA (45) considered the branching true bone formation, with fat cells and connective tissue, in his case to be a sequal to an old interlobular fibroid pneumonia. ANSPERGER (46) and SCHUMACHER (47) likewise assign an inflammatory origin to the arborescent bone-formations, while RATYNSKA (48) found no evidence of any preceding inflammation and regards the branching bone spicules as remnants of anlage misplaced during fetal life.

In one recent case of pulmonary chondroma (7), intratracheal lipiodol injection was employed. The left bronchus was penetrated normally, but the right contained only a slight trace of the iodized oil in the first portion of the right primary bronchus. At autopsy, a pedunculated intra-bronchial chondroma almost completely obliterated the bronchial lumen. The bronchi distal to the incomplete obstruction were filled with pus and the lung showed extreme emphysema, bullous in type, at the periphery. In the diagnosis of the chondromas associated with the bronchi, the employment of lipiodol offers interesting diagnostic possibilities.

Roentgenographic studies have been made in but four cases of pulmonary chondroma, including our own second case. In REBOUL'S case, the roentgenologist's diagnosis was echinococcus cyst or dermoid cyst. In the case reported by CAUSSADE, et al, the diagnosis was bronchiectasis, with obstruction of the right primary bronchus. In EDLING'S (12) case, roentgen-ray examination showed an egg-shaped mass, with sharply circumscribed periphery, separated from the thoracic wall and heart by air-containing lung tissue. His diagnosis was echinococcus cyst. Eight months later the shadow had doubled in size, but had retained its ovoid form, and the diagnosis remained unchanged. EDLING further states that there was no eosinophilia or other evidence of echinococcus infestation. In our case, the roentgenographic appearance suggested echinococcus cyst.

According to the literature, solitary echinococcus cyst of the lung is much more commonly encountered than primary pulmonary chondroma, and the roentgenographic appearances are quite similar. Hence, such errors in interpretation are easily understood, especially if one is influenced by the laws of probabilities. However, since the chief problem in diagnosis seems to exist between the chondromas

and echinococcus cysts, the writers would like to propose certain differential criteria which they have derived from a retrospective study of their own cases and those in the literature.

As regards the appearance of the periphery, the chondromas are invariably nodular, even though these irregularities may be slight, while the echinococcus cyst is either perfectly smooth or presents slight inflammatory infiltrations in the immediately adjacent lung tissue. In pulmonary chondromas, peripheral inflammatory infiltrations are practically unknown. The nodular periphery of the chondromas can best be seen with stereoscopic films.

Of equal importance is the patchy, irregular distribution of lime-salts in the chondromas, due either to simple calcification of the cartilage matrix or to true ossification. Calcification of the laminated chitinous lining membrane of the echinococcus cyst is very rare, and if it did occur would probably be a more uniform process.

Probe-puncture might be employed in doubtful cases, but the probability of spreading a walled-off process to healthy lung and pleura in the case of echinococcus cyst should deter one from utilizing this simple procedure.

If the nodular periphery is present, together with an irregularity of radiopacity due to the haphazard calcification or ossification, in the absence of clinical evidence of taenia echinococcus infestation, one should think of pulmonary chondroma.

The practical importance of differentiating between chondromas and echinococcus cysts is at once evident, since the chondromas usually possess no clinical significance, while surgical interference is frequently indicated in pulmonary echinococcus cysts.

In the two cases (EDLING; REBOUL) in which pulmonary chondromas were removed surgically, the preoperative diagnosis was echinococcus cyst. In EDLING'S case, an apple-size chondroma was removed by BORELIUS (49). The patient enjoyed an uneventful convalescence and was discharged as cured. In REBOUL'S case, an ostrich-egg size chondroma was removed from the inferior half of the right lung. The patient suffered severe shock and died 6 hours postoperative. In this case, the large chondroma had produced severe respiratory symptoms which entirely incapacitated the patient. The autopsy revealed no other cause of the respiratory embarrassment.

Tabulated Abstracts of Reported Cases

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
1	Abrikosoff, Russky Arkhiv Patologii, St. Petersburg, 1902, XIV, 1013—1019.	F		(*Uremia. Cirrhosis of liver.*) Just beneath pleura of right lung, a hard, grayish-white, semi-transparent, round mass, somewhat larger than a pea, and of cartilaginous consistency. Pleural surface smooth and glistening. Lung tissue normal save for slight edema. On section, tumor fell away from surrounding tissue.	Major portion of mass showed cartilaginous architecture. Cartilage cells normal in appearance and distribution. Calcium deposits around many cells. Cartilage divided into compartments by vascular connective tissue, within which were areas of adipose tissue. Many epithelial formations in the connective tissue septa. Many cyst-like spaces, lined by epithelium, either cuboidal or columnar in type, but usually the latter. Some of the epithelial cells appeared in compact nests. Connective tissue capsule similar in structure to the septa; in this, too, were found the same epithelial configurations. Large amount of elastic tissue in cartilage. Designated tumor, «adenochondroma.»
2	Adams, Trans. Path. Soc., London, 1850—51, III, 58—60.	M	66	(*Died of injuries.*) Irregular, nodulated cartilage growth, $^{3}/_{4}$ by $1\,^{1}/_{2}$ inches, in upper lobe of left lung. Partly subpleural, but almost completely surrounded by lung tissue. On section, picture of enchondromatous ossification, the cartilaginous basis being studded with bone.	Cartilage, with islands of bone(?) with distinct lacunae; destitute of canaliculi. (Describes calcified cartilage matrix, with cartilage cells. No positive evidence of bone.)
3	Adamson, Proc. Path. Soc. Great Britain and Ireland, Jour. Path. and Bact., Cambridge, 1912—13, XVII, 108—109.	M	9	(*Osteomyelitis of femur.*) In root of upper lobe of left lung, the upper division of left bronchus and immediate branches surrounded by a hard, irregular mass, decidedly calcareous in parts, and about walnut-size. No chondromata elsewhere.	Hyaline cartilage, showing calcification in places. Through it run bronchi which are normal in structure as far as the muscularis mucosae. Strands of loose connective tissue, containing blood, vessels, traverse cartilage.
4	Bleu, Bull. Soc. Anat., Paris, 1847, XXII, 408.	M	59	At summit of right lung, in healthy surroundings, a yellowish-white cartilaginous tumor, adherent to summit of lung by a slender pedicle. No evidence of pleuritis.	

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
5	Borst, Die Lehre von den Geschwülsten, Wiesbaden, 1902, I, 156.			Walnut-size chondroma, in a case of pronounced anthracosis, with complete absence of carbon pigment in the tumor.	
6	Busse, Arch. f. path. Anat., Berlin, 1907, CLXXXIX, 1—11.	M	40	Large, hard tumor almost completely filled right thorax. Lung totally compressed. Infiltrated upper part of lung, so that Busse designated it chondromyxosarcoma. Definitely separated from ribs, sternum, and vertebral column. Largest and most degenerated portion of tumor in upper lobe of lung. No continuity with bronchial cartilages. In part, tumor separated from lung by capsule. Busse concludes that origin may have been in pleura.	Closely arranged cells in a translucent matrix, giving impression of hyaline cartilage. Divided into many compartments by fibrous tissue septa. Areas of mucous connective tissue.
7	Caussade, Sormont and Lacapère, Bull. et. Mém. Soc. Anat. de Paris, 1925, III Série, XLIX, 1299—1307.	M	53	(*Abundant purulent expectoration for several months — 200 to 500 cc. in 24 hours. Diagnosis, bronchiectasis. Intratracheal lipiodol injection thru Rosenthal tracheal fistula. Left bronchi penetrated normally; right contained only a slight trace of iodized oil.*) Autopsy revealed a pedunculated tumor in the right primary bronchus, almost completely obliterating lumen. Tumor size of pulp of 5th finger of adult. Apparently made up of multiple agglomerated smaller masses of cartilaginous consistence. General emphysema of lung, bullous in type at periphery. Bronchi filled with pus. Only one showed dilatation. No purulent process elsewhere in body. Left lung showed only emphysema.	Tumor composed almost entirely of cartilage cells grouped in threes or fours, some disposed in a linear fashion.
8	Chiari, Prager Med. Wchnschr., 1883, VIII, 497—499 (Case One).	F	68	(*Pulmonary emphysema and purulent bronchitis.*) In left lower lobe, multiple saccular bronchi. In one of these bronchiectatic cavities, connected to the wall by a pedicle, a nodular tumor of	Hard deposits were calcified hyaline cartilage; remainder of tumor made up of fat tissue in irregular lobules, with scattered areas of glands. Designated this mixed tumor, »lipo-chondro-adenoma.»

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
				walnut-size — pale yellow in color with many hard, calcium-like deposits.	
9	Ibid. (Case two).	M	70	(*Generalized tuberculosis.*) Multiple bronchiectatic cavities. In a walnut-size cavity in right lower lobe, a whitish-gray, hard tumor, adherent throughout half of its periphery. Smooth surface covered with epithelium. Glandular structure grossly visible, with pea-size cavities containing mucin.	Much gland tissue, with cubical and polyhedral cells, often mucus-containing. Many cystic glandular spaces filled with mucin. Otherwise similar to first case.
10	COURMONT, Mém. et Compt.-Rend. Soc. Scienc. Méd. de Lyon, 1895, XXXV (deux. partie), 13.			(*Recurring asthmiform crises, orthopnea, extreme cyanosis.*) At autopsy, all organs negative except lungs. In apex of left lung, a hard, orange-size cartilage tumor, completely surrounded by a connective tissue capsule, and supplied by a large branch of the pulmonary artery. Periphery of tumor granular, with facetted nodules the size of a small pea. Each granule is hard and enveloped by a connective tissue capsule. Center of osseous consistence. Tumor surrounded by healthy air-containing lung tissue. No other tumors elsewhere.	No microscopical study.
11	DALTON, Trans. Path. Soc., London. 1883—1884, XXXV, 82—83.	M	44	(*Pain in right shoulder and arm for 3 months. Thrombosis of external jugular veins. Edema of right arm.*) Lobulated mass replaced mediastinal glands, and surrounded trachea and large vessels. At anterior border of upper lobe of right lung, just above root, apricot-size tumor extended into mediastinum.	Inner portion made up of hyaline cartilage. Outer portion, including mediastinal mass, fibrocartilage with areas of mucoid degeneration.
12	EDLING, Fortschr. auf dem Gebiete der Roentgenstrahlen, Hamburg, 1917, XXV, 25—28; also BORELIUS and SJÖVALL, Nordiskt	F	40	(*Entered hospital for nervous symptoms. Thorax deformed. Heart displaced to left. X-ray examination showed shadow to left of heart; egg-shaped mass, with sharply circumscribed periphery; separated from*	Cartilage islands surrounded by richly cellular perichondrium and fat tissue. At periphery of fat tissue, many small single nodules containing smooth muscle and lymph nodules. Spaces lined by single layer of non-ciliated

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
	Med. Arkiv, 1915, Afd. I., N:r 12, 1—14.			*thoracic wall and heart by air-containing lung tissue; no pulsations; no connection with mediastinum. Diagnosis: echinococcus cyst. Eight months later, shadow had doubled in size, but retained its ovoid form. No evidence of infiltrative growth. No eosinophilia. Diagnosis unchanged. Operation by* BORELIUS. *Resection of apple-size, round, stone-hard tumor, which reached the basal pleura. Tumor capsule split and tumor was quickly enucleated. Uneventful convalescence. Released as cured.)* Tumor surface divided by depressions into small and large yellowish nodules, resembling fat tissue. No apparent connection with bronchi or surrounding lung tissue. Consists chiefly of cartilage islands, with areas of calcification, surrounded by thin layer of fat-like tissue.	cubical epithelium, giving the single nodules an organoid structure. New nodules appeared to be developing in the form of a roughly papillary, fibroepithelial growth.
13	FELLER, Arch. f. Path. Anat., Berlin, 1921—22, CCXXXV—CCXXXVI, 470—480.	F	66	(*Senile marasmus.*) Tumor, 9 by 11 cm., in middle lobe of right lung, near pleura. Very definite boundary. Separated from surrounding tissue on section. Yellowish, translucent, with small, opaque, white deposits. Bronchial lumen seemed to surround tumor. Papillated surface. Macroscopically, gave the impression of a lipoma.	At periphery, bronchial epithelium, varying from single flattened, nonciliated cells to stratified ciliated epithelium. Some bronchial mucous glands extend into tumor. Epithelium frequently in cell nests, at first giving impression of carcinoma. Tumor for most part made up of fat tissue, devoid of lobulations. In areas, connective tissue, shows myxedematous degeneration. Many fibroblasts and lipoblasts at periphery. Irregular small and large cartilage islands embedded in fat — much larger than normal bronchial cartilage plates — distributed in purposeless fashion. Branches of bronchus appeared to extend deeply into tumor, gradually becoming covered with a simple flat non-ciliated epithelium, with intracana-

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
					licular projections, simulating fibroma intracanaliculare mammae.
14	Foerster, Arch. f. Path. Anat., Berlin, 1858, XIII, 106—107.	M		Two hard bodies, of bean-size, in lung, very close to one another; of stony hardness.	Concentrically calcified cartilaginous matrix, with encapsulated cartilage cells. No enchondromas elsewhere in body.
15	Hart, Zeitsch. f. Krebsforschung, Berlin, 1906, IV, 578—585. (Case one).	M	67	(*Died in diabetic coma.*) Nodular, hazelnut-size tumor in right lower lobe. On section, separated readily from surrounding tissue. No connection with neighboring bronchi.	Round and oval cartilage islands separated by loose connective tissue, fat tissue, various glandular structures, rich blood supply. Mixed with myxofibrolipomatous tissue, parallel strands of low cylindrical epithelial cells with well-defined lumina and many arborizations, some cystic and filled with desquamated epithelium or homogeneous coagulum.
16	Ibid. (Case two).	M	68	(*Diabetes mellitus.*) Walnut-size, hard, nodular, grayish-white and opalescent tumor, with stonehard center, in left lower lobe, near hilus. Near left main bronchus, but not connected with it.	Differed from tumor described above only in character of individual tissues. Myxedematous tissue recedes in importance and in its place a fibrillar connective tissue, rich in capillaries. Multiple individual cartilage islands, with abundant fat tissue. Much old blood pigment. Much poorer in glandular structures.
17	Heschl, Oesterreich. Zeitsch. f. prakt. Heilkunde, Wien, 1862, III, 42—43.	M	25	(*Died of »dropsy«.*) Mulberry-like masses of small osteoid tumors, on pleural surface and deep in lung. 20 to 25 of these in compressed lower right lobe.	Showed true bone structure, with distinct lamellar system. No inflammatory changes about these and no traces as to origin.
18	Hickey, and Simpson. (Case one).	M	62	(*Carcinoma of stomach.*) Hard, spherical, nodular tumor, 12 by 16 mm. in anterior portion of lower lobe of the right lung, situated just beneath the pleura. Encapsulated. Cartilaginous consistence. Separated easily from neighboring lung tissue. No apparent connection with bronchi.	Composed largely of irregular cartilage islands, with calcification of the hyaline matrix. In septa, much myxomatous and fibrous connective tissue, adipose tissue, and branching gland-like spaces lined by simple cubical and columnar epithelium. On one side, the epithelium is stratified and ciliated. Transitions from the stratified to simple epithelium

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
					could be traced. Diagnosis: myxo-fibro-lipo-adenochondroma.
19	HICKEY and SIMPSON. (Case two).	M	58	(*Carcinoma of prostate gland.*) Extremely hard, spherical, nodular, yellowish-white tumor, 5 cm. in diameter, in the antero-inferior portion of upper lobe of right lung, 3 cm. from pleural surface. Definitely encapsulated and separated easily from surrounding lung tissue. Grated on section. Many irregular grayish, translucent islands of cartilaginous consistence, with whitish, stony-hard calcified areas. Reddish-brown vascular areas at one side. Connective tissue and fat tissue in septa.	Cartilage islands, united by cartilaginous bridges, dominate picture. Hyaline cartilage for most part, with patches of fibrocartilage. Irregular lime-salt deposits in cartilage. Central necrosis of larger islands. Small areas of bone formation, with fatty marrow. Loose connective tissue, in part myxedematous, with areas of fat tissue in septa, together with irregular spaces lined by simple cuboidal and columnar epithelium. Myxo-fibro-lipo-osteo-adenochondroma.
20	JANSEN, Inaug. Diss., Bonn, 1914.	M	45	Well-defined subpleural nodular mass, of walnut-size, with distinct connective tissue capsule, yellowish-white color, and tough, elastic consistency. Cut surface bluish-white and shining like ordinary cartilage, with scattered whitish streaks.	Young and old cartilage islands, staining with varying intensity, producing a mottled appearance. Lighter areas consist of hyaline cartilage, rich in cells, and areas of connective tissue and blood vessels. Darker areas are calcified, particularly at the periphery of the cartilage lobules. No true ossification.
21	LAKIN, Arch. Middlesex Hosp., London, Clin. Series, 1912, XXV, 37—39.	F	53	(*Hepatic cirrhosis.*) Pigeon's egg size tumor, one-eighth inch beneath pleura, in mediastinal aspect of lower lobe, just below root of left lung. Not attached to larger bronchi. Sharply defined from surrounding lung tissue. Bluish, translucent appearance on section.	Consists of hyaline cartilage. No regularity in arrangement of cells. For the most part, cartilaginous substance was sharply marked off from the rest of the lung tissue, but at one spot, transitional spindle cells appeared to gradually merge into the connective tissue of lung. Areas of myxomatous change in connective tissue.
22	LEGG, Trans. Path. Soc., London, 1874—75, XXVI, 11—13; also St. Bart. Hosp. Rep., 1875, XI, 77.	M	39	(*No history.*) In left lower lobe, ½ inch below the pleural surface, oval, nodular tumor, contained in a cyst-like cavity. Cut easily, save for center, which was calcified. No other tumors elsewhere.	After decalcification, microscopical study showed only cartilage and fibrous tissue: no bone. Tumor surrounded by a capsule similar to renal fibrous capsule.

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
23	LEBERT, Physiologie Pathologique, Paris, (Chez J. B. Ballière), 1845, II, 213—215.			Barth found at necropsy, a yellowish-white tumor, with an irregular surface, 2 by 3 cm., between the two pulmonary lobes. At first thought to be a diseased bronchial lymphnode. Greater part made up of cartilage, with some fibrous tissue and vessels.	True cartilage, with much fat tissue, fibrous tissue and blood vessels.
24	LESSER, Arch. f. Path. Anat., Berlin, 1877, LXIX. 404—409.	F	78	(*Mitral and aortic insufficiency.*) In the lower lobe of left lung, near middle of mediastinal surface, an S-shaped tumor, 15 × 5.5 × 2.5 cm. In lower half, covered only by thickened pleura; upper end as high as entrance of left primary bronchus; lower border at diaphragm. Surface lobular, many of walnut-size, connected by connective tissue strands. Surface yellow and opaque, with many red areas. Many bone-like areas. Between tumor and bronchi, several mm. of compressed lung tissue.	Many areas gave strong amyloid reaction. Much loose, vascular connective tissue, masses of hyaline cartilage, fibrocartilage, osteoid tissue, true bone and bone marrow. At periphery of tumor, compressed lung tissue showing brown induration. (Marked splenic amyloidosis. Syphilitic hepatitis.)
25	VON LIECHTENSTEIN, Inaug. Diss., Göttingen, 1868.	M	64	(*Trauma. Dysentery.*) Hazelnut-size tumor of cartilaginous hardness in lung substance, immediately under calcified apical pleura. Surface nodular, with millet-seed size protrusions; oval; 20 mm. × 14 mm.; yellowish-white color, with faintly bluish hard areas. Distinct connective tissue capsule. Lay loosely in lung parenchyma, united to it by pedicle. No connection with bronchi.	Cartilage tissue, for the greater part fibrocartilage, with a few areas of hyaline matrix. Encapsulated cartilage cells throughout entire mass — frequently so closely packed that matrix could not be recognized. In many areas calcification of matrix. Made up of single cartilage nodules, separated by connective tissue septa. Scattered throughout were small and large fat bodies. Surrounding gland tissue entirely normal.
26	LINSER, Arch. f. Path. Anat., Berlin, 1899, CLVII, 281—297.	M	13	(*Pleuritis.*) In left lung, an encapsulated, brownish-yellow tumor, 20 × 16 × 9—11 cm., with indistinct lobular structure. In part very soft, but towards periphery, many rough, firm, whitish, fairly transparent islands.	Lobular structure with thick connective tissue septa. In lobules, flat to cuboidal epithelium in glandular cyst-like structures, with scattered islands, of hyaline cartilage and scattered strands of smooth muscle. Excessive stroma reaction appeared sarcomatous in areas.

No	Reference	Sex	Age	Gross Description	Microscopical Examination
27	McGLUMPHY, Jour. Cancer Research, 1924, VIII, 482—498. (Case one).		51	(*Auto-intoxication. Delirium tremens.*) Chief tumor situated 3 mm. below lung surface. Approximately 2 cm. in diameter and of chondromatous consistency. Indistinct lobulation. A few smaller tumors in neighborhood.	Lobulation more pronounced. Single roundish units, sometimes connected by thin chondromatous bridges. Units separated by vascularized stroma, containing abundant epithelial elements in duct-like double rows. Central degenerative changes in largest masses. No true ducts; duct-like structure is produced by conglomeration of closely packed chondromatous bodies, the surface of each covered by a thin epithelial layer. Epithelium cuboidal and cylindrical, bearing cilia in central portion of tumor. No transition between epithelium of tumor and that of lung.
28	Ibid. (Case two).		75	(*Marasmus. Diffuse chronic bronchitis.*) Spherical cartilaginous tumor, 1 ½ cm. in diameter, in lower lobe of left lung, with periphery of tumor adjacent to pleura, next to hilum. Whitish. Divided by deep fissures into multiple single areas. Small areas of calcification.	Marked lobulation. Units separated by connective tissue and epithelial-lined clefts. Epithelium varies from non-ciliated cuboidal to ciliated cylindrical. Thin layers of fat tissue between epithelium and cartilage.
29	Ibid. (Case three).		53	(*Coronary arteriosclerosis.*) Hard, spherical subpleural tumor in lower lobe of left lung, 3 cm. in diameter, situated in anterior-inferior area of mediastinal surface of the lobe. Separated from pleura by thin layer of lung tissue. Light blue, translucent. Made up of conglomeration of roundish units, separated either by vascularized connective tissue. No pathological change in surrounding lung tissue.	Conglomeration of single, cartilaginous units, the smallest with a diameter of 2 mm., frequently connected by cartilaginous bands. Some areas of calcium deposit. Spaces between cartilage islands contain either edematous, richly vascular connective tissue or fat cells. Interstitial tissue contains many duct-like structures lined by simple cubical or cylindrical epithelium, some of which are cyst-like and contain mucoid substance. No ciliated epithelium. Connective tissue capsule continuous and bore no relationship to immediately adjacent lung tissue.
30	Ibid. (Case four).		41	(*Embolus of left femoral artery; mitral stenosis and insufficiency; thrombosis of left auricular appendage; multiple emboli.*) Tumor, 2	Made up of hyaline cartilage with many shrunken, deformed cells. Liquefaction necrosis in center. Multiple areas of mucinous degenera-

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
				cm. in diameter, of cartilaginous consistency. Irregular contour with numerous fissures. 9 mm. cavity in center. Tumor separated from pleura by thin membrane.	tion. In angles between cartilage units, numerous little ducts with narrow lumina, lined by simple cubical epithelium — giving impression of atrophying structures. In a few places there is transition of these ducts to lung alveoli.
31	Reboul, Thèse, Lyon, 1919.	M		(*Bronchitis, right-sided pleuritis, anemia; radiograph showed ostrich-egg size tumor in inferior part of right lung resting on diaphragm. Diagnosis: hydatid cyst or dermoid? Operation. Removal of tumor. Death, 6 hours postoperative. Autopsy.*) Very hard tumor, 15·5 × 11·5 cm.; weighed 780 G. Surface resembled cerebral hemispheres, with convolution-like elevations produced by cartilage masses. Grayish-white color, with ivory-colored islands of osseous consistence. Remainder of lung entirely normal. No essential pathology elsewhere in body.	Large cartilage islands, surrounded by fat tissue, large irregular blood spaces, and lamellae of bone, with arachniform bone corpuscles, devoid of Haversian canals. Most of cartilage islands show at some point osseous transformation, particulary at periphery, resembling transitions seen in epiphyses.
32	Reissig, Inaug. Diss., Würzburg, 1892.			Cherry-size cartilage tumor in lung and pleura.	Contained connective tissue, fat tissue, bone and bone-marrow, as well as cartilage.
33	Ritter, Inaug. Diss., Würzburg, 1897.	M		Near sharp border of lower lobe of right lung, hard, whitish-blue, walnut-size tumor, with nodular, lobular elevations on surface. Center of tumor calcified. Completely surrounded by capsule, 2—3 mm. thick, continuous with pleura.	Consists of multiple smaller and larger bodies, made up of pure hyaline cartilage, with well-developed, encapsulated cartilage cells. Relatively dense connective tissue, with round cell infiltration, between islands of cartilage. Surrounding lung tissue rich in carbon pigment, but tumor and compressed lung tissue at the periphery show no anthracosis.
34	Schultz, Cited by Busse, loc. cit.	M	69	In edematous right lung, between 8th and 9th rib, kidney-shaped cartilage tumor, located on pleura, in form of a sac. In apex, other pea-size cartilaginous nodules.	

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
35	SCHUMANN, Inaug. Diss., München, 1914.	M	53	(*High grade dyspnea. Myocardial insufficiency.*) Tumor size of man's head, weighed 12 pounds. Stone-hard consistency. Surface showed nodular prominences. Left lung completely compressed, and separated with difficulty from tumor, particularly in hilus region. In two areas, tumor was interwoven with bronchial wall. Nodular eminences penetrated wall of pulmonary vein, but endothelium was everywhere intact.	Homogeneous ground substance, with cartilage cells devoid of capsules. Ground substance extensively calcified. No bone formation.
36	SIEGERT, Arch. f. Path. Anat., Berlin, 1892, CXXIX, 413—425.			Intrabronchial chondroma, 23 × 32 mm., 8 mm. below bifurcation of right primary bronchus, in the lower main bronchus. Appeared to completely fill the lumen of the bronchus. Grossly, simulates bony tissue.	Surrounded by emphysematous lung tissue with numerous corpora amyloidea on one side and by bronchial wall on the other aspect. Tumor composed of connective tissue and epithelial structures, and abundant cartilage, with many cavernous blood spaces. Designated »choudro-angioma.» Apparently arose in bronchial perichondrium.
37	TAPIE, Le Midi Médical, Toulouse, 1892, I, 358—388.		28	In the antero-external part of left lower lobe, a cavity the size of a hen's egg. Adjacent to cavity, a bony mass the size of the palm of the hand. On section, composed of two parts: one very hard, red, resembling cancellous bone; the other, surrounding it and giving the impression of very hard fibrous tissue. Scattered through both lungs, many grayish-white neoplastic masses.	Osteoma in immediate contact with epithelial neoplasm. Many osteoblasts and areas of typical bone architecture. Multiple adenocarcinoma nodules in lungs.
38	VIGOUROUX and HÉRISSON-LAPARRE, Bull. et Mém. Soc. Anat. de Paris. 1912, XIV, 377—380.	M	52	Approximately spherical, 15 cm. in diameter, tumor in left thorax, attached by a pedicle to the infero-medial surface of the left lung, from which it appears to have arisen. Firm, yellowish-white. Cartilaginous consistence at periphery, calcareous or osseous in central portion. Left bronchus normal throughout.	At the periphery, cartilage cells pressed one against the other, forming multiple islands, with vascular connective tissue and chondroblasts.

No.	Reference	Sex	Age	Gross Description	Microscopical Examination
39	WAGNER, Archiv. f. Heilkunde, Leipzig, 1861, II, 280—282.	M	64	(*Carcinoma of stomach.*) Cherry size, grayish-red tumor in posterior part of lower lobe of left lung, one inch from the pleura. Separated easily from surrounding structures. Irregular papillated excrescences on surface. Grayish-yellow, hard center. Located near a middle-sized bronchus, but not connected with it in any way.	Nucleus of tumor consisted of reticular cartilage, with distinct encapsulated cells. Numerous fat cells. In the hyaline ground substance were many elastic fibers, some embedded in a mucous substance.
40	WILKS, Trans. Path. Soc, London, 1861—62, XIII, 27—28.	M	28	(*No history.*) Left lung atrophied. At root, cartilaginous tumor involved bronchial nodes and left bronchus. Apparently originated from bronchus.	Microscopical verification of cartilaginous nature.

SUMMARY

1. The results of a roentgenological and pathological study, based upon a report of two cases of primary pulmonary chondroma and an analysis of data obtained from previous reports of thirty-eight similar cases, are presented.

2. Primary lung chondromata undoubtedly occur with greater frequency than a review of the literature would indicate.

3. Progress in roentgenology has stimulated interest in these tumors.

4. No case has ever been properly interpreted roentgenographically.

5. Macroscopically, the tumors usually appear to be made up of multiple islands of cartilage, separated by vascular connective tissue and adipose tissue. Calcification or ossification of the cartilage occurs in most instances. The tumors are almost invariably surrounded by normal lung tissue.

6. Two gross characteristics of these tumors which possess differential diagnostic importance are the invariable nodular, lobulated periphery and the patchy, haphazard calcification or ossification.

7. Microscopically, in addition to the calcified or ossified cartilage, connective tissue and fat tissue, one usually finds complex glandular structures in the septa between the cartilage units, lined by cuboidal or columnar epithelium. Smooth muscle has been described in a few cases.

8. The majority of the tumors were located just beneath the pleura. In but six of the forty cases was there any close association with the bronchi.

9. These complex tumors probably have their origin in displaced bronchial anlagen, since all of the histological elements found in them are normal components of the bronchi.

10. The few cases which have been studied roentgenologically have been diagnosed echinococcus cyst. The lobular, nodular periphery and haphazard calcification or ossification of the pulmonary chondromas, together with an

absence of clinical manifestations of taenia echinococcus infestation, should serve to distinguish these tumors.

11. The practical importance of such differentiation is at once evident when one considers the great difference in the treatment of the two diseases.

ZUSAMMENFASSUNG

1. Die Verff. berichten über die Resultate einer röntgenologischen und pathologischen Untersuchung, basiert auf Grund zweier mitgeteilter Fälle von primärem Lungenchondrom und einer Analyse der aus früheren Publikationen über 38 ähnliche Fälle erhaltenen Daten.

2. Primäre Lungenchondrome kommen zweifellos in grösserer Frequenz vor, als nach Durchsicht der Literatur zu schliessen wäre.

3. Die Fortschritte der Röntgenologie haben das Interesse an diesen Tumoren angeregt.

4. Kein Fall ist noch röntgenographisch richtig gedeutet worden.

5. Makroskopisch scheinen die Tumoren gewöhnlich aus multiplen Knorpelinseln zu bestehen, die durch gefässreiches Bindegewebe und Fettgewebe von einander getrennt sind. In den meisten Fällen findet man Kalzifikation oder Ossifikation des Knorpels. Die Tumoren sind fast immer von normalem Lungengewebe umgeben.

6. Zwei differentialdiagnostisch wichtige Hauptcharakteristika dieser Geschwülste sind ihre stets knollige, gelappte Kontur und die in unregelmässigen Flecken auftretende Verkalkung oder Verknöcherung.

7. Mikroskopisch findet man, ausser verkalktem oder verknöchertem Knorpel, Bindegewebe und Fettgewebe in den Septa zwischen den einzelnen Knorpeln gewöhnlich Komplexe von drüsigen Gebilden, deren Lumen mit kubischem oder Zylinderepithel ausgekleidet ist. Bei einigen wenigen Fällen sind glatte Muskeln gefunden worden.

8. Die Mehrzahl der Tumoren war unmittelbar unter der Pleura lokalisiert. Nur bei 6 von 40 Fällen bestand eine enge Verbindung mit den Bronchien.

9. Ihren Ursprung haben diese komplizierten Tumoren wahrscheinlich in verlagerten Bronchialanlagen, da alle in ihnen gefundenen histologischen Elemente normale Bronchusbestandteile sind.

10. Die wenigen Fälle, die röntgenologisch genauer untersucht worden sind, wurden als Echinokokkuszysten diagnostiziert. Die lappige, knollige Kontur und die unregelmässige Verkalkung und Verknöcherung der Lungenchondrome zusammen mit dem Fehlen klinischer Anzeichen für eine Taenia-echinococcus-Injektion hätten zur Unterscheidung dieser Tumoren zu dienen.

11. Die praktische Wichtigkeit dieser Differentiierung leuchtet sofort ein, wenn man den grossen Unterschied in der Behandlung der beiden Zustände bedenkt.

RÉSUMÉ

1. Les auteurs communiquent les résultats d'une étude radiologique et pathologique, basée sur l'analyse de deux cas de chondrome pulmonaire primitif et sur les considérations résultant des observations antérieures de 38 cas analogues.

2. Le chondrome pulmonaire primitif est incontestablement une affection plus fréquente que ne pourrait le faire supposer une revue de la bibliographie.

3. Les progrès réalisés par la radiologie ont accru l'intérêt offert par cette catégorie de tumeurs.

Fig. 1.

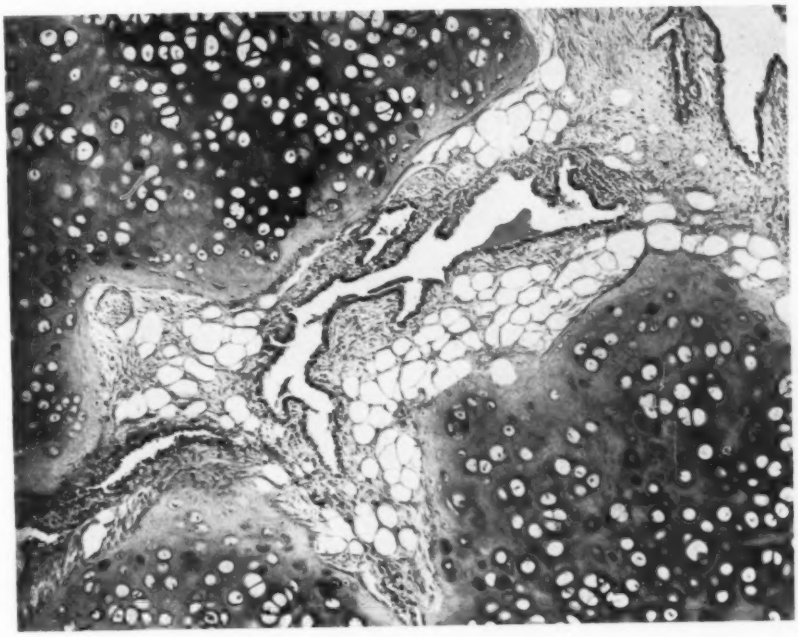

Fig. 2.

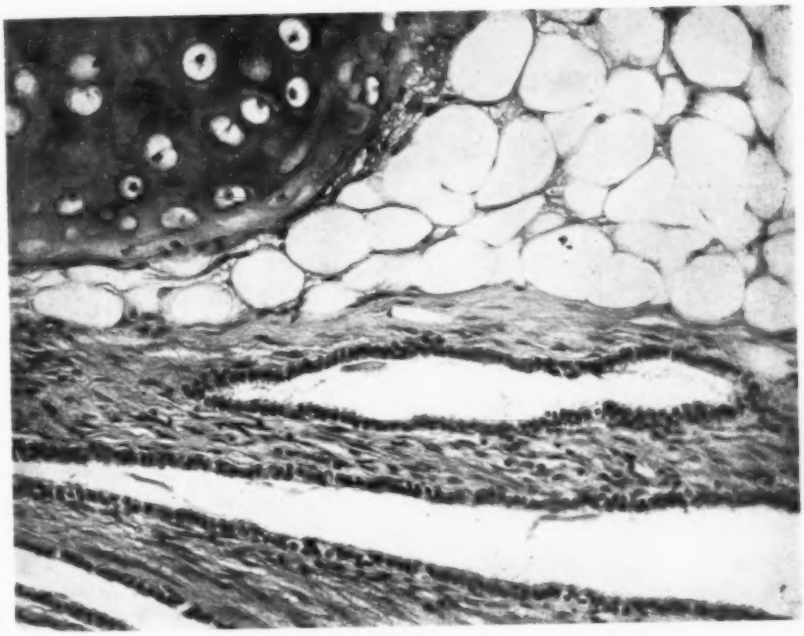

Fig. 3.

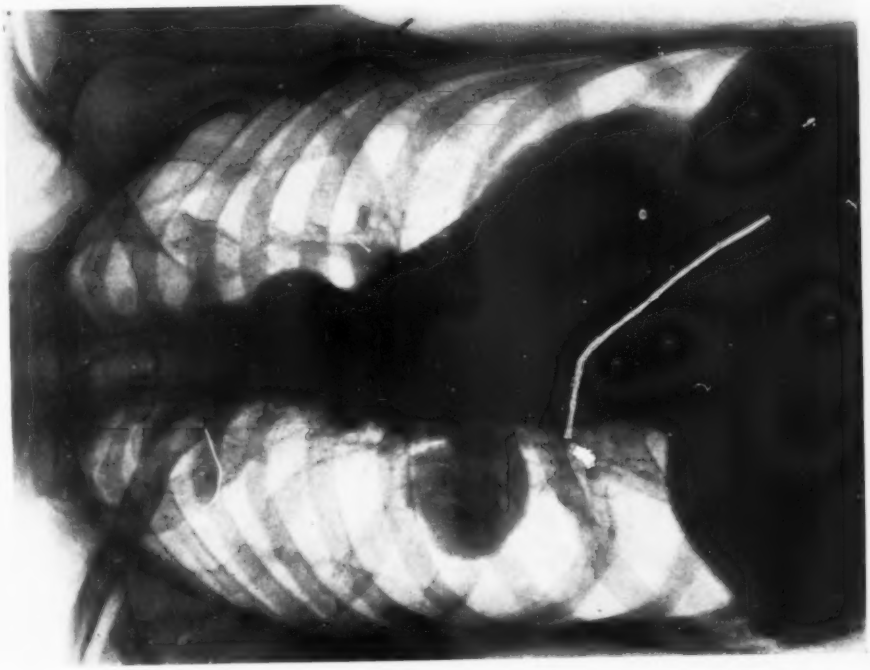

Fig. 4.

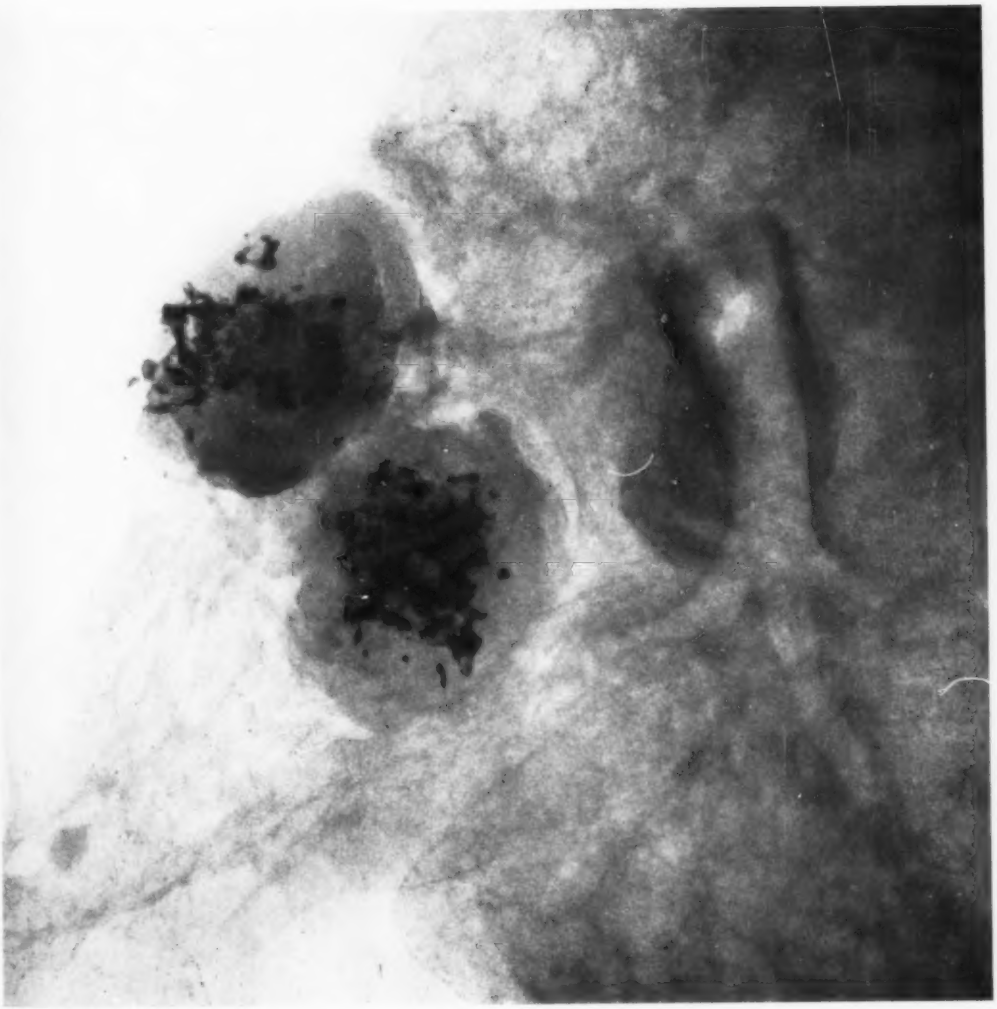

Fig. 5.

Fig. 6.

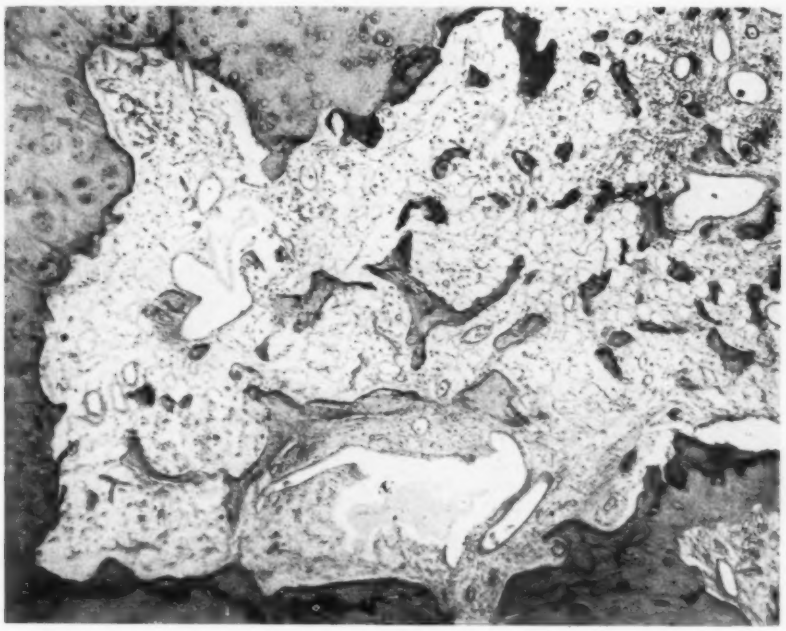

Fig. 7.

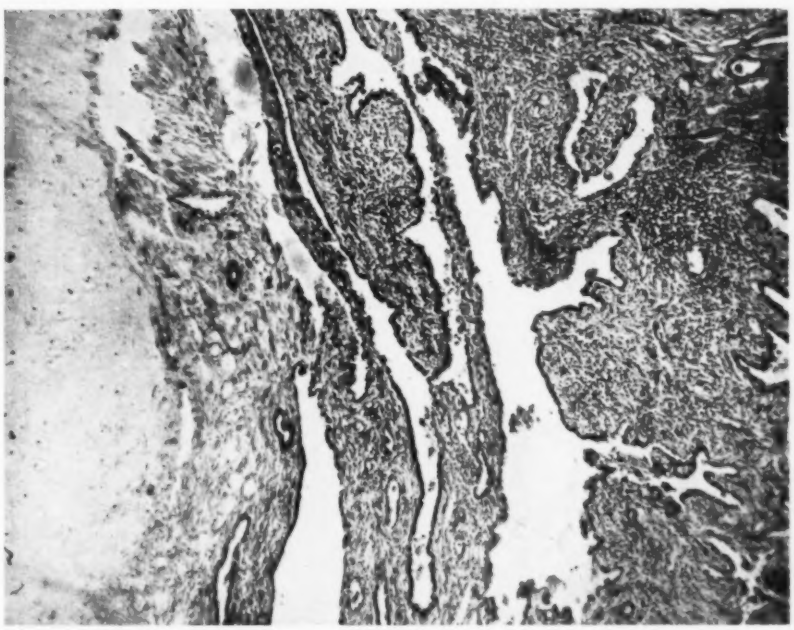

Fig. 8.

4. Aucun cas n'a jusqu'ici été interprété radiologiquement.

5. Au point de vue macroscopique, ces tumeurs paraissent généralement constituées par des îlots multiples de cartilage, séparés par des travées de tissue conjonctif vascularisé et de tissue adipeux. On observe dans la majorité des cas une calcification ou une ossification du cartilage. Les tumeurs sont presque invariablement englobées dans du tissu pulmonaire normal.

6. Ces tumeurs présentent deux particularités caractéristiques, d'une grande importance au point de vue du diagnostic différentiel: un aspect invariablement noduleux, lobuleux de la périphérie, et, une ossification ou calcification disséminée sans ordre.

7. Au point de vue microscopique, et en dehors du cartilage ossifié ou calcifié, du tissu conjonctif et adipeux, on observe généralement des formations de nature glandulaire dans les septa qui séparent les masses cartilagineuses, formations revêtues d'un épithélium cylindrique ou cuboide. Dans quelques cas, on décrit des muscles lisses.

8. Le plus grand nombre de ces tumeurs étaient localisées immédiatement au-dessous de la plèvre. Dans six cas seulement sur quarante, on notait une communication close avec les bronches.

9. Ces tumeurs complexes ont probablement leur origine dans des formations bronchiques ectopiques. Les éléments histologiques dont elles se composent se retrouvent en effet dans la structure normale des bronches.

10. Les quelques cas soumis à l'examen radiologique ont été pris pour des kystes à échinocoques. La structure lobulée, nodulaire de la périphérie des chondromes pulmonaires, la présence d'îlots disséminés d'ossification ou de calcification jointes à l'absence de tout signe clinique d'échinocoques permet de distinguer ces deux affections.

11. L'importance pratique de cette différenciation est manifeste quand on considère la différence qui existe entre les traitements de ces deux affections.

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LEGENDS

Figure 1. *Case One.* Photomicrograph showing papilliferous glandular structures, with low columnar epithelium; cartilage islands with lime salt deposits in the ground substance; myxomatous connective tissue and fat.

Figure 2. *Case One.* Large cartilage islands, rich in calcium salts, with young connective tissue, adipose tissue and irregular, branching glandular structures in the septa between the cartilage units.

Figure 3. *Case One.* Higher power photomicrograph showing in detail the low columnar epithelium of the gland-like spaces, as well as the connective tissue, adipose tissue and a portion of a calcified cartilage island.

Figure 4. *Case Two.* Radiograph of chest, showing chondroma of right lung. The slight nodular irregularities at the periphery, the sharply circumscribed character of the tumor, and the irregular distribution of the calcified and ossified areas, are well shown.

Figure 5. *Case Two.* Radiograph of right lung after removal from the body. The film shows the difference in density of the cartilage islands, sharply contrasted with the calcified and ossified areas towards the center of the tumor.

Figure 6. *Case Two.* Photograph of right lung, showing tumor after section. The irregular, nodular periphery is well seen, with the whitish chalk-like calcium deposits. Towards the center is the myxomatous connective tissue, fat, and marrow substance with the whitish bone trabeculae. The darkest areas are made up of vascular bone marrow. The distinct capsule is clearly seen.

Figure 7. *Case Two.* Transformation of cartilage to bone, with vascular, fatty marrow. The calcium salts have been almost completely removed by decalcifying solution.

Figure 8. *Case Two.* Irregular, somewhat papilliferous glandular structures, lined by cuboidal epithelium. A portion of a large decalcified cartilage island is seen towards the left, with a few scattered fat cells at the periphery. The connective tissue is quite mature and is diffusely infiltrated with lymphocytes.

AUS DER STRAHLENTHERAPEUTISCHEN ABTEILUNG (LEITER: PROF. DR. L. HALBERSTAEDTER)
DES UNIVERSITÄTS-INSTITUTES FÜR KREBSFORSCHUNG AN DER CHARITÉ IN BERLIN.
(DIREKTOR: GEH.RAT PROF. DR. FERD. BLUMENTHAL.)

EXPERIMENTELLER BEITRAG ZUR POSTOPERATIVEN STRAHLENBEHANDLUNG BÖSARTIGER GESCHWÜLSTE HINSICHTLICH WUNDHEILUNG UND VERHÜTUNG ÖRTLICHER REZIDIVE

von

L. Halberstaedter und *Alb. Simons*

Wir haben in den letzten Jahren in zunehmendem Masse zur Behandlung von inoperablen Carcinomen die Elektro-Coagulation angewendet. Hierbei haben wir, besonders bei kleineren, abgrenzbaren Herden, die Exstirpation mit dem Funken der nachfolgenden Verschorfung vorausgeschickt. In fast allen Fällen handelte es sich um Rezidive vorher in anderer Weise, meist chirurgisch, behandelter Tumoren, jedenfalls aber um solche Fälle, bei denen jetzt chirurgischerseits die Exstirpation mit dem Messer aus irgend welchen Gründen angelehnt worden war. Nach jeder Coagulationsbehandlung haben wir prinzipiell eine Nachbestrahlung mit Radium- oder Röntgenstrahlen bezw. eine Kombination beider sofort angeschlossen. Wir haben also noch vor vollständiger Abstossung des Coagulations-Schorfes mit der Strahlenbehandlung begonnen oder in die durch die Lichtbogen-Operation geschaffene Wundhöhle sofort Radiumkapseln eingelegt. — Auf die Technik und Dosierung soll an dieser Stelle nicht eingegangen werden.

Wir hatten uns nun bei diesen Massnahmen die Frage vorgelegt, ob eine derartige Nachbestrahlung zweckmässig sei, sowohl im Interesse der Wundbehandlung als auch zur Verhütung auftretender örtlicher Rezidive.

Der erste Punkt war auf Grund der von uns in diesen Fällen gemachten Beobachtungen dahin zu beantworten, dass eine wesentliche Störung in der Wundheilung bei unserer Dosierung nicht zu verzeichnen war. In manchen Fällen, besonders in denen, bei welchen das betreffende Gebiet schon früher wiederholt mit Strahlen behandelt war, bildete sich ein gelber, fest haftender, zäher Belag,

der zu seiner völligen Abstossung längere Zeit gebrauchte, aber schliesslich doch guten Granulationen Platz machte, die sich schnell überhäuteten, nachdem der Belag erst vollständig abgestossen war. Die entstandenen Narben waren als durchaus gut zu bezeichnen. Sie waren in der Regel dünn und elastisch. Keloidartige Verdikkungen, wie sie sonst häufig nach grösseren Hautdefekten auftreten, fehlten zumeist völlig. Unsere Beobachtungen decken sich in dieser Hinsicht mit den von L. FREUND über den Einfluss von Röntgenbestrahlungen auf den im Gange befindlichen Vernarbungsprocess von frischen, offenen Wunden (Wien. kl. W. Jg. 39, N:o 11. 1926) gemachten Feststellungen. Wir sind der Ansicht, dass die etwas längere Heilungsdauer der Wunden im Hinblick auf die zu erwartende günstigere Narbenbildung von völlig untergeordneter Bedeutung ist.

Schwieriger war die Frage zu beantworten, ob nicht die verhältnismässig günstigen örtlichen Resultate, die wir in vielen Fällen beobachten konnten, auch ohne die Nachbestrahlung zu erreichen gewesen wären, also allein auf das Konto der vorgenommenen Coagulation zu setzen sind. Es ergab sich bei der Beurteilung dieses kombinierten Verfahrens dieselbe Schwierigkeit, die sich ja auch für die Beurteilung des Wertes der postoperativen Bestrahlung überhaupt ergibt. — Um diese Frage auf statistischem Wege zu lösen, ist eine ausserordentlich grosse Zahl von Patienten mit langer Beobachtungszeit notwendig, und auch dann gibt der verschiedene Verlauf, der auch sonst in den einzelnen Fällen eintreten kann, die Möglichkeit der Missdeutung.

Wir haben daher zur Lösung dieser Frage einen anderen Weg beschritten, und in einigen Fällen, bei denen es sich um grössere Flächen handelte, unter scharfer Abdeckung nur einen Teil des durch Coagulation zerstörten Carcinomherdes bestrahlt. Über den Verlauf eines derartigen Falles, der unserer Meinung nach den Wert der Nachbestrahlung in eklatanter Weise zu demonstrieren imstande ist, soll im Folgenden berichtet werden:

Frau E. M. 49 Jahre alt, erlitt am 18. Mai 1925 einen Stoss gegen die linke Brust. Sie beobachtete dann, dass sich die Brustwarze nach und nach einzog. Später wurde vom Arzt eine Verhärtung in der Brust festgestellt, die Patientin wurde zur Operation ins Krankenhaus geschickt. Amputation der Brust mit Ausräumung der Achselhöhle am 15. September 1925. Am 13. November 1925 zur Nachbestrahlung geschickt. Wir stellten damals eine Infiltration der linken Supraclaviculargrube fest und verabreichten der Patientin in der Zeit vom 2.—11. Dezember 1925 eine Röntgenserie. Der vorgeschlagenen zweiten Bestrahlungsserie entzog sich die Kranke. Am 19. April 1926 stellte sich die Patientin mit einer Hautmetastasen*aussaat* rings um die Narbe wieder vor. In der Achselhöhle fühlte man in der Tiefe einen kirschgrossen Knoten. Am 20. und 21. April wurde das Knötchengebiet an der Brust am Röntgenapparat unter 6 mm Al Filter mit $2 \times {}^1/_2$ E. D. bestrahlt. An denselben

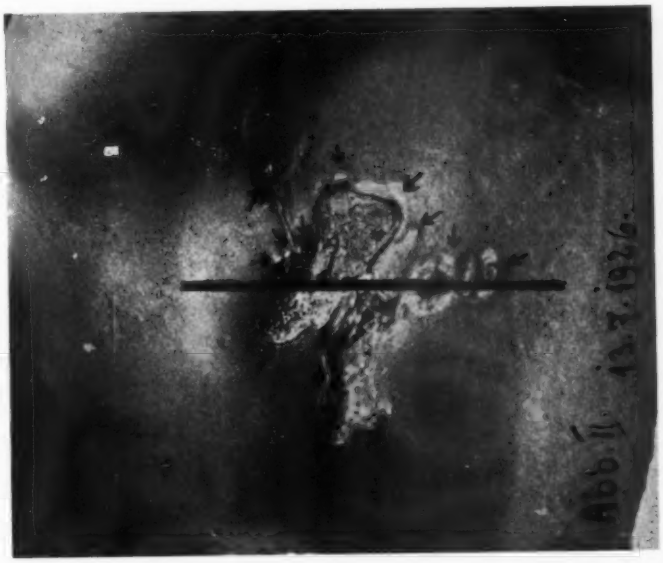

Abb. II.

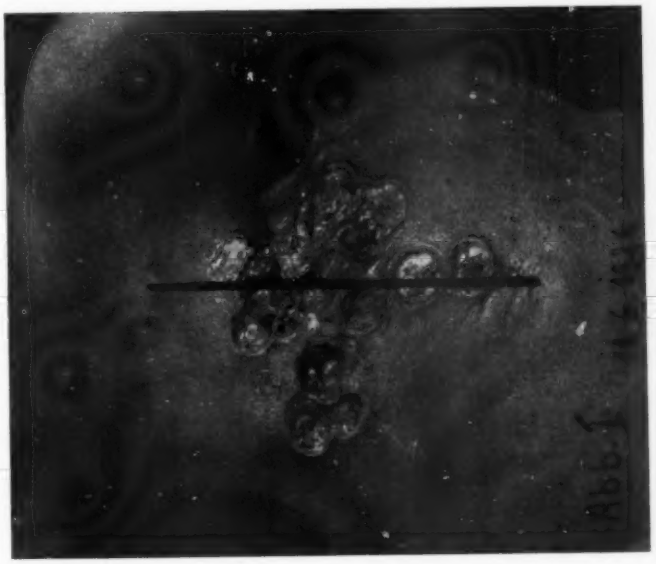

Abb. I.

Tagen wurde die Achselhöhle mit einem Radiumpaket behandelt. Am 28. Mai war keine Beeinflussung der Hautknötchen festzustellen, in der Achselhöhle hingegen war der Tumor verschwunden. Am 2. Juni wurden die Hautknötchen in Narkose mittels Diathermie coaguliert, wobei jedes einzelne Knötchen sorgfältigst bis weit in die Tiefe hinein und nach den Seiten hin in Angriff genommen wurde, um möglichst bis ins Gesunde zu gelangen. Einige confluierende Knötchen der Haut des vorderen Achselhöhlengebietes excidierten wir mittels Lichtbogens, um Material zur mikroskopischen Untersuchung zu gewinnen. Das Aussehen des Operationsgebietes am 11. Juni zeigt Abb. I. An diesem Tage bestrahlten wir die mediale Hälfte am Röntgenapparat mit 1 E. D. unter 1 mm Al Filter, wobei die laterale Hälfte mit einer Bleigummiplatte scharf abgedeckt wurde (in einer Linie, die durch den Strich auf der Abbildung gekennzeichnet ist). Am 13. Juli stellte die Patientin, die inzwischen verreist war, sich uns erstmals wieder vor. Die bestrahlten Hautpartien zeichneten sich durch ein Erythem deutlich von der unbestrahlten Haut ab. Die Geschwürsfläche des unbestrahlten Gebietes zeigte frisch aussehende, rote Granulationen, die den Geschwürsgrund bis zum Niveau der Hauträndern ausfüllten und grösstenteils noch etwas überragten. An den bestrahlten Partien hingegen lag der Geschwürsgrund deutlich etwas unter dem Hautniveau, zeigte einen feinen, kontinuierlichen, gelben Belag, der sich nur an einigen kleineren Stellen offenbar abgestossen hatte, so dass feinkörnige, rote Granulationen zu Tage traten. Die Geschwürsränder zeigten sowohl im bestrahlten als auch im unbestrahlten Gebiete deutliche Vernarbung, die allerdings im unbestrahlten Teile etwas weiter vorgeschritten war als im bestrahlten. Auffallend war auch, dass die Narben des bestrahlten Gebietes zwar fest aber dünn, elastisch und blass war, im Gegensatz zu der roten, derben, starren, stellenweise keloidartig verdickten Narbenbildung auf der unbestrahlten Hälfte. Während auf der medialen Seite des Operationsfeldes nichts Rezidivverdächtiges festgestellt werden konnte, zeigten sich in den Narbenrändern des lateralen Teiles einige, durch ihre mehr braunrote Farbe auffallende, knötchenförmige Verdickungen (auf Abb. II durch Pfeile gekennzeichnet). Auch die Granulationen zeigten stellenweise ein sehr tumorverdächtiges Aussehen. Wir excidierten das unterste der am Narbenrande befindlichen Knötchen sowie Granulationen aus dem oberen Teile der fast ganz geschlossenen, von der Lichtbogenoperation herrührenden Wunde unter der Achselhöhle. Der histologische Befund ergab einwandfrei, dass an beiden Stellen ein Rezidiv vorlag. Wir beobachteten die Kranke noch bis zum 23. 7. 26 weiter und konnten ein deutlich fortschreitendes Wachstum der Knötchen, sowohl in den Narbenrändern als auch in der granulierenden Geschwürsfläche des unbestrahlten Teiles feststellen, und ebenso das Auftreten von neuen Hautknötchen weiter unterhalb des coagulierten Bezirkes, aber ausschliesslich im unbestrahlten Bezirk. Wir nahmen alsdann alles Carcinomverdächtige erneut in Strahlenbehandlung. *In dem nach der Elektro-Coagulation bestrahlten Geschwürs- und Hautbezirk ergab sich bis zu diesem Zeitpunkte absolut nichts Rezidivverdächtiges*, die Rezidivaussaat schnitt scharf mit der Abdekkungsgrenze ab.

Ob auch die nachbestrahlte Partie *später* Carcinomrezidive zeigen wird, ist für die Beurteilung des Falles gleichgültig. Jedenfalls ist in einwandfreier und bisher in dieser Art nicht gezeigten Weise bewiesen, dass durch die nach der Coagulation ausgeführte Röntt-

genbehandlung die Entwicklung eines örtlichen Rezidivs auf alle Fälle verzögert, wenn nicht gänzlich verhindert worden ist. *Wir folgern daraus nicht nur die Berechtigung sondern auch die Notwendigkeit einer postoperativen Nachbestrahlung in geeigneter Weise.*

ZUSAMMENFASSUNG

Es wurden in mehreren Fällen grössere, offene Wundflächen nach Diathermieoperation von Carcinomherden in der Weise nachbestrahlt, dass nur eine Hälfte den Strahlen ausgesetzt, die andere mit Blei geschützt war.

Es zeigte sich:

1. dass zwar eine gewisse Verzögerung der Wundheilung in den nachbestrahlten Bezirken eintritt, die resultierenden Narben aber in der Regel besser sind als die in den nicht bestrahlten Teilen;
2. dass in einem Falle nach Ablauf eines Monats der nicht postoperativ bestrahlte Teil des Operationsgebietes zahlreiche Rezidivherde aufwies, während die nachbestrahlte Partie rezidivfrei geblieben war.

SUMMARY

In several cases where removal of carcinomatous masses with diathermy had left large, open ulcers, it was so arranged that one half of each ulcer was irradiated while the second half was protected by lead. It was thereby shown:

1. that, although there was a certain amount of delay in the healing of the post-irradiated area, the resulting scar was, as a rule, in a sounder condition than in the parts not so treated;
2. that in one case, after the lapse of one month, there occurred numerous recurrent foci in the part not exposed to irradiations after the operation while the treated part remained free from such recurrences.

RÉSUMÉ

Sur des plaies ouvertes, fort étendues, consécutives à l'opération diathermique de foyers cancéreux, les auteurs ont pratiqué des irradiations, qui ont été appliquées de telle sorte que la moitié de la plaie était exposée à ces irradiations, l'autre moitié étant protégée par des plaques de plomb. Ils ont constaté:

1. que malgré un certain retard de la cicatrisation dans la région irradiée, les cicatrices obtenues étaient généralement de meilleure nature que dans les parties non irradiées;
2. que, dans un cas, après un délai d'un mois, la partie non irradiée du champ opératoire présentait de nombreux foyers de récidive, tandis que les parties irradiées étaient absolument exemptes de phénomènes de cet ordre.

AUS DEM RÖNTGENINSTITUT ZU LUND, OBERARZT L. EDLING

RÖNTGENOLOGISCHE SKELETTVERÄNDERUNGEN BEI MORBUS GAUCHER[1]

von

Sven Junghagen

(Assistent)

(Tabulæ XL—XLVI).

Im Frühjahr 1924 erhielt die hiesige pediatrische Klinik einen Fall von Splenomegalie, der als Morbus Gaucher diagnostiziert und an die chirurgische Klinik zur Splenektomie abgegeben wurde, da die Diagnose auch pathologisch-anatomisch verifiiert werden konnte. Während der Rekonvaleszenz begannen sich Symptome vom Skelettsystem einzustellen, die sich allmählich als mit erheblichen organischen Veränderung verknüpft herausstellten. Durch das freundliche Entgegenkommen von Prof. v. KLERCKER habe ich Gelegenheit erhalten die Krankengeschichte des Kindes einzusehen und sei hier als Einleitung ein kurzer Auszug aus derselben wiedergegeben.

Ped. Journ. 149/24. Mädchen Elsa J., 3 Jahre, aufgen. d. $^{22}/_{4}$ 24. Eltern gesund, ein 2 Jahre alter Bruder ebenfalls. Keine verstorbenen Geschwister. Der Bauch soll seit der ersten Lebenswoche gespannt und gross gewesen sein. Im Übr. normaler Säugling bis zu $1^{1}/_{2}$ Jahren. Ging zu Beginn des zweiten Jahres. Lernte früh sprechen und spricht jetzt vollkommen rein. Seit zwei Monaten glauben die Eltern dass sich ihr Zustand verschlimmert hat. Der Bauch wurde gespannter und grösser. Stuhl normal. Im letzten Monat täglich aber härter. Gestern und heute Erbrechen.

Status: Normal entwickeltes Kind, etwas mager. Eine gewisse, wenn auch geringe gräuliche Blässe der Haut. Kein Icterus, höchstens ein gewisser bräunlicher Anstrich der Backen, des Bauches sowie der Beine. Zerstreute, punktförmige subkutane Blutungen (Flohbisse?). Pharynx blass. Mundschleimhaut und Givae nichts Bemerkenswertes. Keine Blässe der Lippen oder Konjunktivae. Keine Verdickung der Conj. bulbi. Auf den lateralen Teilen des Halses bis zu erbsengrosse Adeniten in mässiger Menge. Keine vergrösserten Drüsen in den Axillen oder Inguina.

Lungen: Klarer Ton. Atmungslaut normal. *Herz:* reine Töne.

Bauch: gespannt, aufgetrieben, misst um den Nabel 51 cm, grösste Weite 53,5 cm. Kein Wellenschlag. Die ganze linke Seite des Bauches wird von der Milz erfüllt, die bis in das kleine Becken hinabreicht und die mit scharfem, festem Rand und gleichmässig glatter Oberfläche mehr als 1 cm rechts des Nabels palpiert wird; wenigstens eine deutlich palpierbare Incisur. Aus-

[1] Der Fall wird in Acta Pædiatrica 1927 von Herrn Prof. Kj. af Klercker unter dem Titel Beiträge zur Kenntnis des Morbus Gaucher behandelt.

füllung unter dem rechten Rippenrand. Dämpfung in der rechten Flanke. Aufrechtsitzen bereitet der Pat. wegen der grossen Milz Schwierigkeit.

Gallenfarbstoffe im Harn nach Gmelin und Rosenbach sowie Hammarsten neg.

Urobilin neg. *Urobilinogen* (Aldehyd Ehrlich) schwach pos. *Bilirubin* (Hijmans van der Bergh) im Blutserum neg. — sowohl direkt wie indirekt. Normale Zahnformel. Den $^{24}/_{4}$ sowohl Urobilin- wie Urobilinogenprobe neg. Blutbild normal. Am $^{26}/_{4}$ während 4 Min. angelegte Stauungsbinde hat keine Hautblutungen zur Folge. Stichprobe neg. Keine pathologischen Formen von roten Blutkörperchen. 0,01 Alt-Tuberkulin gibt keine Reaktion.

Röntgenuntersuchung der Lungen: (Dr. Y. Olsson) Pleurasinus frei. Vom linken Hilus verläuft aufwärts-lateral, der Richtung von C_2 folgend, ein dünnes Bündel von Schattenstrichen mit eingelagerten Flecken. Die Zeichnung ist dort oben etwas unregelmässig, spärlich fleckig (Tbc. ?). Im linken Hilus vielleicht eine bohnengrosse Drüse, die zur broncho-pulmonalen Drüsengruppe gehört.

$^{28}/_{4}$. Wassermann neg. $^{3}/_{5}$. Husten. Bei der Auskultation in liegender Stellung einzelne zerspreute Ronchi in beiden Lungen. Sonst 0.

$^{6}/_{5}$. *Differentialzählung:* Neutrophile Leukozyten 38 %, Lymphozyten 58 %, Übergangsformen 4 %, Makro-, Mikro- und Poikilozytose. Ein kernhaltiges rotes auf 200 weisse. Die Erytrozyten im allgemeinen von normaler Farbstärke, keine Polychromatophilie oder Punktierung, einzelne etwas hyperchrom gefärbt.

$^{9}/_{5}$. Während der letzten Tage war Pat. bedeutend apathischer, wollte liegen und schlafen oder schlummern. Schwitzt stark. Einzelne Rasselgeräusche in beiden Lungen. — Das Kind wurde auf Begehren der Eltern entlassen.

Am $^{13}/_{10}$ 24 abermals aufgenommen. Allg.-zust. wenig beeinflusst. Fortwährend kein Icterus. Einige kleinere Suggilationen an verschiedenen Stellen der Haut. Stauungs- und Stichprobe ergeben nichts Bemerkenswertes. *Herz:* Weicher systolischer Blaslaut an der Basis. *Lungen:* 0. *Bauch*: Gespannt und aufgetrieben. Die linke Seite des Bauches wird von der Milz eingenommen, die mit scharfem und festem Rand gut 3 fingerbreit rechts der Nabelebene palpiert werden kann und nach unten bis zur Symphyse reicht. Die Leber wird 1 fingerbreit unterhalb des Rippenbogens palpiert. Bauchfang 63 cm. *Urobilinogen* (Ehrlich) pos. Übrige Gallen- und Harnproben neg. *Bilirubin im Blut* $\frac{0{,}20}{200\,000}$ (indirekt).

$^{17}/_{10}$. *Röntgenuntersuchung:* (Olsson) Jetzt sind in den Lungen keine Veränderungen sichtbar. $^{18}/_{10}$. Die Haut der Dorsalseite der Unterarme und Hände zeigt eine schwache Braunpigmentierung, während die Volarseite sowie die Finger und Oberarme deutlich lichter sind; keine scharfe Grenze der Pigmentierung an den Backen. Am scharfen Milzrand gewahrt man deutlich zwei kleinere Incisuren.

$^{30}/_{10}$. *Splenectomie* auf der chir. Abt. (G. Petrén). Medianschnitt. Geringe Menge Ascites. Die Leber vergrössert aber im übr. von normalem Aussehen. Die Milz ohne Adherenzen, zeigt mehrere lichte Infarkten. Exstirpation leicht ohne Blutung. Gewicht der Milz 1 150 g, Länge 21 cm, Breite 14.5 cm, Höhe 8,5 cm. Geheilt per primam. *P. A. D.* Die normale Milzstruktur ist fast ganz verschwunden und nur einzelne Follikel sind vorhanden. Das Pulpagewebe ist vollständig durchsetzt von grossen, lichten, leberzellenähnlichen Zellen, die am ehesten endothelialen Charakter aufweisen, in Strichen

und Kolben wachsen und vom Milzsinus auszugehen scheinen. Diese Zellen haben einen verhältnismässig kleinen, oft auf die Kante gestellten Kern, sowie reichliches wenig gefärbtes Protoplasma. Mit Sudan III färben sie sich nur schwach rotbraun. Mit der Weigertschen Markscheidefärbung erhält man dagegen eine deutlich blauschwarze Färbung, was auf das Vorhandensein von mit Myelin verwandten Stoffen (Phosphatiden) deuten soll. Die weissen, infarktähnlichen Partien scheinen dadurch zustande gekommen zu sein, dass hier die grossen hellen Zellen besonders dicht gelegen sowie degeneriert sind, worauf eine kräftige fibröse Reaktion folgte, die die Reste dieser Zellen einschloss. *Diagnose:* Idiopatische, grosszellige Splenomegalie — Typus Gaucher (Dr. A. LINDAU).

Pat. kommt am $^{7}/_{11}$ wieder in die pediatrische Klinik, wo einzelne grobe Rasselgeräusche in beiden Lungen festgestellt werden konnten. *Differentialzählung* ergibt nichts Bemerkenswertes. Sechs kernhaltige auf 100 weisse. Der-Allg.-zust., der anfangs zieml. stark beeinflusst war, verbesserte sich allmählich, sodass sie nach 5 Wochen ein rosiges Aussehen zeigte. Appetit gut. Die Pigmentierung nahm ab und konnte an Händen und Unterarmen beobachtet werden. Grösse der Leber unverändert. Hat erst während der letzten Tage selbständig gehen wollen. *Diff.-zahlung* am $^{15}/_{12}$: Leukozyten 44 %, Lymphozyten 51 %, Übergangsformen 5 %. Am $^{29}/_{1}$ 25 wurde die Pat. in der chirurg. Abt. aufgenommen, da die Eltern merkten, dass sie sich nicht auf den linken Fuss stützen konnte. Auszug aus dem Status: Hält den Fuss in leichter Flexion. Alle Bewegungen des l. Hüftengelenks sind erheblich beeinträchtigt. Die übrigen Gelenke normal.

Röntgenuntersuchung am $^{13}/_{2}$ (Dr. JUNGHAGEN): Keine Veränderung der Hüftgelenke, doch ist eine Andeutung zur Coxa valgastellung in beiden Hüftgelenken vorhanden, da sich der Winkel zwischen Collum und Diaphyse 145° nähert.

Bei der Wiederaufnahme in die ped. Klin. schrie Pat. gerne und hatte Husten, besonders während der Nacht; dieser nahm an Intensität zu und zeigte eine Andeutung zu Anfällen. Keine Reprisen wurden beobachtet (Pertussis?). — Einzelne Ronchi rechts hinten. Am $^{7}/_{3}$ Leukozyten 10 %, Lymphozyten 84 %, Übergangsformen 6 %.

Am $^{27}/_{3}$ Rtg. (Dr JUNGHAGEN): Sämtliche Skeletteile zeigen einen bedeutend verminderten Kalkgehalt und zwischen den dünnen, aber doch schärfer hervortretenden Kortikaliskonturen und der Mittelpartie in den Diaphysen ist ein auffallender Kontrast vorhanden. Die Spongiosa ist überall grobmaschig mit stark hervortretenden spärlichen Spongiosabalken. Die Diaphysen sind von dicht nebeneinander liegenden Verdünnungen durchsetzt, die an einigen Stellen scharf begrenzt, an anderen in einander übergehen, also konfluieren. Im Humerus und Femur treten sie am stärksten hervor; sie können dort in ihrer ganzen Ausdehnung wahrgenommen werden, doch sind hiervon sämtliche Epi- und Metaphysen ausgenommen. Die Verdünnungen sind von Graupen- bis Bohnen- und Mandelgrösse. Im oberen Teil der Tibiadiaphysen sind die Verdünnungen mehr streifenförmig und erstrecken sich zwischen groben Spongiosastrichen herab bis zur Mitte der Tibiae. Entsprechende Veränderungen sind auch

in den Fibulae sichtbar. Im Metacarpalknochen sind gleichfalls kleinere Verdünnungen bemerkbar. In den Hüftgelenken und Beckenknochen gewahrt man keine Veränderungen. Die Kortikaliskonturen sind überall gut erhalten und es ist keine periostale Reizung zu sehen.

Am $^{19}/_{11}$ 25 kam die Pat. zur Nachuntersuchung. Haut und Gesichtsfarbe waren unverändert. Korpulenz gut. Es ist ihr schwer gefallen den linken Fuss zu bewegen und sie hat keine Tendenz zu aktiver Beweglichkeit gezeigt. Im Rückgrat hat sich ausserdem ein gelinder Gibbus in der Lumbalregion entwickelt. *Röntgenuntersuchung* (JUNGHAGEN): Eine erneute Untersuchung verschiedener Skeletteile zeigt eine erhebliche Progression des destruktiven Prozesses. Der Epiphysenkern im Caput femoris im linken Hüftgelenk ist jetzt teilweise verschwunden und es verbleibt ein grösseres laterales Fragment und ein mediales Konglomerat von graupenähnlichen kleineren, die einen oberen Begrenzungsrand für die Epiphyse bilden; der Abstand zwischen dieser und der Collumgrenze ist erheblich kürzer als auf der gesunden Seite, weshalb eine Kompression des Epiphysenkernes (Caput) stattgefunden haben muss. Die Knorpelspalte ist von normaler Breite. Das Collum femoris erscheint auf dieser Seite gröber und breiter sowie kürzer, fortwährend in etwas Coxa valgastellung. Die früher in den Femurdiaphysen beobachteten Verdünnungen haben beträchtlich an Dicke und Ausbreitung zugenommen und reichen an gewissen Stellen bis zur Corticaliskontur hinaus; letztere ist unterbrochen worden, was an der Medialseite beim Übergang zwischen dem mittleren und unteren Drittel der Femurdiaphyse gut beobachtet werden kann. Durch Erhöhung der Anzahl Verdünnungen hat der Knochen ein wurmstichiges Aussehen erhalten. Der rechte Femur hat durch eine periostale Reizung oder organisierte subperiostale Blutung auf der Seite der Diaphyse ein plumperes Aussehen erhalten als der linke.

Die Spongiosazeichnung im Beckenknochen zeigt gleichfalls Zeichen für pathologische Veränderungen, indem sie stark trabekuliert und netzförmig mit groben Spongiosastrichen zwischen dünnen Spatien versehen ist.

Von sämtlichen Lumbalwirbeln zeigt nur L_3 normale Höhe und gleichmässig scharfe Begrenzungskonturen. Die übrigen sind alle, mehr oder weniger, in der Form eines Zusammenbruches deformiert, der in der Mittelpartie der Wirbel am ausgeprägtesten ist; diese zeigen also von beiden Seiten eine Exkavierung. Die Corticaliskontur ist etwas eingedellt und ungleichmässig, erscheint aber überall gut erhalten. In den Mittelpartien der Wirbel sind auch hier verdünnte Gebiete vorhanden, die den in den Diaphysen in den lan-

gen Röhrenknochen ähneln. Am stärksten deformiert ist L_4, der in seiner Mitte nur ungefähr die Hälfte der Höhe der vorderen Kontur misst. Die Knorpelspalten sind von normaler Höhe und die zu beiden Seiten von L_4 gelegenen erscheinen wegen der Einsenkungen in diesem Wirbel breiter als normal. In der Thorakalwirbelsäule sind vollkommen analoge Veränderungen mit Zusammensinterungen von Th_6 und Th_{12} vorhanden.

Die Veränderungen im Humerus zeigen ebenfalls eine sehr starke Progression und die Kalkarmut hat hier einen sehr beträchtlichen Grad erreicht. Die Verdünnungen in den oberen Teilen der Diaphysen haben konfluiert und zwischen diesen verläuft eine äusserst spärliche, grobmaschige Spongiosazeichnung. Auch in den Unterarmknochen sind Verdünnungen sichtbar.

$^{23}/_{3}$. Der Zustand der Pat. scheint sich seit der letzten Untersuchung verbessert zu haben. Hat an Gewicht zugenommen und ein rosiges Aussehen erhalten. Ist etwas lebhafter und bewegt sich mehr selbständig. Auch in der Dorsalwirbelsäule hat sich eine Kyphose ausgebildet, sodass der Thorax eingesunken erscheint.

Röntgenuntersuchung (JUNGHAGEN): Die destruierenden Veränderungen in den Hüftgelenken sind vorgeschritten, sodass vom linken Caput nur eine schmale obere Randzone längs der früheren oberen Fläche übrig ist. Die Knorpelspalte ist noch immer gleich breit wie auf der rechten Seite. Auch in der Thorakalregion der Wirbelsäule ist die Destruktion erheblich vorgeschritten und die meisten Wirbel zeigen Veränderungen in der Form von verminderter Höhe und verdünnten Gebieten in ihren zentralen Partien. Die Konturen der Wirbel sind beibehalten und die Knorpelspalten sind von gleicher Breite wie früher. Durch den Zusammenbruch der Wirbel ist im oberen Teile der Wirbelsäule eine Knickkyphose mit Zentrum in diesem Teile zustande gekommen.

Das reticulo-endotheliale System ist ein im ganzen Körper verbreitetes Gewebe, das zum grössten Teil in Milz, Leber, Knochenmark, Lymphdrüsen, Nebennieren und Hypophyse gelegen ist. Die Zellen bekleiden die Wände der Blut- und Lymphgefässe und ihrer Kapillaren. Die biologischen Funktionen des R. E. Ss. stehen mit der Blutkörperchenbildung und dem Blutkörperchenzerfall, entzündlichen Prozessen, der Immunkörperbildung u. a. Stoffwechselprozessen in intimem Zusammenhang und es ist daher zum grössten Teil an jenen Stellen gelegen wo diese stattfinden. Die Zellen zeigen verschiedene spezifische Reaktionen, indem sie verschiedene vital injizierte Färbstoffe in sich aufnehmen (GOLDMANN). Bei gewissen pathologischen Zuständen werden diese Zellen einer grosszelligen Hyperplasie mit Ansammlung und Auflagerung von grossen Mengen Lipoiden und

lipoidhaltigen Substanzen unterworfen. ANITSCHKOW und CHALATOW haben experimentell durch Cholesterinfütterung von Kaninchen eine Cholesterinämie mit Anhäufung dieses Stoffes im R. E. S. hervorgebracht. Morphologisch gleich zeigt sich die Lipoidzellenhyperplasie die man bei der durch Morbus Gaucher hervorgerufenen Stoffwechselstörung erhält. In diesem Falle hat sich aber der Stoff, den die Zellen erhalten, als ein Cerebrosid erwiesen, das von LIEB mit Kerasin identifiziert wurde. Ob es sich um eine Infiltration resp. Resorption oder um eine Protoplasmahyperplasie handelt ist nicht entschieden.

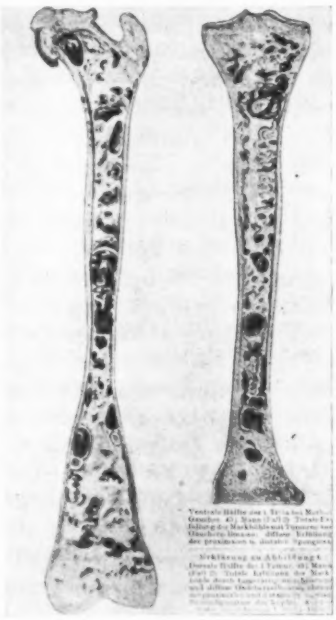

Fig. a.

Morbus Gaucher ist eine seltene Krankheit, die familiär auftreten kann. Ihre Dauer kann, wenn der Tod nicht im frühen Kindesalter eintritt oder eine intercurrente Krankheit hinzustösst, ziemlich bedeutend sein und sich im allgemeinen über Jahrzehente erstrecken. Das klinische Bild tritt oft mit einer enormen Milzanschwellung, Lebervergrösserung ohne Ascites, Dyspepsie, Pigmentierung der Haut, Tendenz zu Blutungen der Schleimhäute, anämische Zustände sowie Neuralgien und atritischen Beschwerden zutage. PICK hat über die Krankheit 1924—25 eine grosse Monographie veröffentlicht und ist der erste der ihre Lokalisation im Skelettsystem festgestellt hat. ZADEK hat allerdings etwas früher einen Fall von Morbus Gaucher mit Veränderungen im Knochensystem publiziert, doch war die Diagnose für die dort vorhandenen Skelettveränderungen, wie ZADEK selbst angibt, von PICK gestellt worden.

Je länger die Krankheit dauert, desto grössere Möglichkeiten sind natürlich dafür vorhanden, dass das Skelettsystem affiziert wird. Es hat sich indessen gezeigt, dass es Fälle mit einer Dauer von 30—40 Jahren gibt, die keinerlei oder nur äusserst spärliche Skelettveränderung aufweisen; andererseits hat man sehr junge Fälle mit stark ausgebreiteten Zerstörungen angetroffen. Ein Beispiel für diese letztere Kategorie bildet gerade der hier oben relatierte Fall. PICK glaubt demnach eine gewisse individuelle Disposition für Morbus

Gaucher im Knochensystem zu »metastasieren» und gleichzeitig eine familiäre Disposition für denseblen feststellen zu können. Er hat u. a. einen Geschwisterkreis von 7 Kindern beobachtet; zwei Schwestern starben sehr jung an einer unbekannten Krankheit und fünf Brüder, von denen vier starben, waren mit Morbus Gaucher behaftet, der in sämtlichen Fällen zu bedeutenden Zerstörungen und deformierenden Veränderungen im Skelette führte.

Die pathologisch-anatomischen Veränderungen, die im Skelett vorhanden sind, sind vor allem bedeutende Einlagerungen von »Gauchergewebe» in die Marklöcher in den langen Röhrenknochen (Riesel) und diese Einlagerungen können einen solchen Grad erreichen, dass sie zu einer Druckatrophie und zum Untergang der Corticalis führen; letztere kann papierdünne werden und spontanfrakturieren. Im allgemeinen verbleibt die Corticalis ungebrochen und die Oberfläche gleichmässig. Durch die bedeutende Anhäufung kann ferner eine Diskonfiguration des Knochens zustande kommen, indem die Diaphyse aufgetrieben und erheblich verdickt wird. Auch in der spongiösen Substanz, sowohl in den Epiphysen, in der Diploe im Kranium wie in den Wirbelkörpern u. a. Stellen findet eine Einlagerung von Gauchersubstanz mit Untergang der Spongiosa statt. Dieser Untergang kann, was die Epiphysen in den Gelenken betrifft, zum Zusammenbruch der Gelenkköpfe und zu grossen sekundären artritischen Veränderungen Anlass geben. In den Wirbelkörpern erfolgt ein Zusammensintern mit darauffolgender Gibbusbildung. Eine Einlagerung in die chondrogenen Teile des Skelettes hat dagegen nicht festgestellt werden können. Die Intervertebralscheiben behalten auch zum grössten Teil ihre normale Höhe und Form bei.

In der spongiösen Substanz gleichwie in der Corticalis sind eingelagerte, verschieden grosse, gut abgegrenzte »Noduli» (von Kugel- oder Ellipsenform) mit Gauchergewebe vorhanden, die bei zunehmender Grösse konfluieren können. Auch zwischen den verschiedenen Knochenbalken hat man mikroskopisch Gaucherzellen beobachten können, die diese auseinander treiben.

Der oben relatierte Fall, über dessen Diagnose man nicht im geringsten Zweifel sein dürfte, da sie sowohl klinisch wie pathologisch-anatomisch festgestellt worden ist, weist — wie die Röntgenuntersuchung zeigt — ausgedehnte Skelettveränderungen auf. Nachuntersuchungen haben gezeigt, dass sie sich in steter Progression befinden. Diese Nachuntersuchungen sind von umso grösseren Wert, da bisher keine Angaben über bei Röntgenuntersuchungen beobachteten Skelettveränderungen veröffentlicht worden sind.

Vor allem wird der Untersucher von der Kalkarmut frappiert, die über das ganze Skelett verbreitet ist und die bei jeder Untersuchung

zugenommen zu haben scheint. Die Cortikaliskontur ist auffallend dünn, besonders in den langen Röhrenknochen, wo sie in der medialen unteren Partie des linken Femurs auf einer ca. 5 mm langen Strecke defekt erscheint. Die Metaphyse im unteren Teile des rechten Femur ist in ihrer Form ausserdem plumper als die entsprechende Partie auf der linken Seite.

Die Spongiosazeichnung zeigt ein spärlicheres und gleichzeitig gröberes Aussehen als normal, sodass sie trabekuliert erscheint. Sowohl in den Epiphysen wie in den Diaphysen sind graupen-erbsengrosse Defekte in der Form gut begrenzter Verdünnungen vorhanden, die ebenfalls bei jeder Untersuchung an Grösse zugenommen und teilweise konfluiert haben. Durch die dicht neben einander liegenden »Löcher» hat der Knochen ein charakteristisches *wurmstichiges Aussehen* erhalten. Auch grössere Defekte sind sichtbar, indem der Epiphysenkern im linken Hüftgelenk allmählich zerstört wird, sodass er bei der letzten Untersuchung stark an einen Perthes im 2ten Stadium erinnerte. Die ausgesprochendsten Veränderungen haben jedoch die Wirbelkörper sowohl in der Lumbal- wie Thorakalwirbelsäule erlitten. Die Wirbelkörper sind in der Form einer Zusammensinterung deformiert, sodass sie länger geworden sind, ihre Konturen sind unregelmässiger und unebener aber doch beibehalten. Im allgemeinen erhält man den Eindruck, dass zuerst das Zentrum des Wirbels nachgegeben hat und dann die periphereren Teile. In der Thorakalwirbelsäule verursacht ein Zusammenbruch von 5—7 Thorakalwirbeln einen kräftigen Gibbus. Auffallend ist, dass die Knorpelspalten ihr normales Aussehen beibehalten haben und in gewissen Fällen sogar breiter als normal erscheinen, nämlich an den Stellen des das Zentrum des Wirbels zusammengesunken ist und die Kontur wo Wirbels mit sich gezogen hat.

Gegen den Hintergrund der früher relatierten pathologisch-anatomischen Veränderungen betrachtet lassen sich diese Beobachtungen leicht analysieren. Die Kalkarmut im Skelette und die dünne Cortikalis beruhen auf einer starken Infiltration von Gauchergewebe in das Knochenmark mit sekundärer Beeinflussung des Skelettes in der Form einer Atrophie. Die plumpe Form der unteren rechten Femurmetaphyse dürfte ebenfalls auf der starken Infiltration beruhen, die die Corticalis vor sich herschiebt und ausbuchtet. Die trabekulierte Zeichnung kann vielleicht auf einer Infiltration von Zellen zwischen die Knochenbalken beruhen, wodurch diese auseinander getrieben werden. Die kleinen Defekte im Knochen sind diesen isolierten kugel- und ellipsenförmigen Infiltraten, die den Knochen usurieren, zuzuschreiben. Bei Morbus Gaucher können indessen derartige »Entkalkungen» nach Pick auch durch dislozierte Lymphknoten hervorgerufen werden.

Die starke Zerstörung der Wirbelkörper kommt gleichfalls durch eine successive Einlagerung von »Gauchergewebe» zustande, was zu einer verminderten Tragkraft dieser führt. Es folgt ein Zusammenbruch der Wirbelkörper, was rascher oder langsamer verlaufen kann, je nach der Progression der Einlagerung. Ausserdem können durch die Belastung und veränderten statischen Verhältnisse Blutungen und Nekrosen im Gauchergewebe entstehen, was den Verlauf der Zerstörungen beschleunigt. Bei den wiederholten, von mir vorgenommenen Untersuchungen der Wirbelsäule habe ich die Behauptung PICKS nicht verifiieren können, dass der Zusammenbruch der Wirbelkörper in den Randpartien und im vorderen Teil des Wirbelkörpers beginnen sollte. Ich glaube eher festgestellt zu haben, dass die Zusammensinterung zentral im Wirbelkörper beginnt, während die Randpartien viel länger erhalten bleiben. Gleichwie PICK am pathologisch-anatomischen Präparate keine regenerativen Veränderungen hat feststellen können, haben derartige auch bei dieser Untersuchung nicht konstatiert werden können. Der destruktive Prozess hat für jede Untersuchung stetig zugenommen, indem der Kalkgehalt des Skelettes vermindert wurde, die Defekte in den verschiedenen Skelettteilen haben an Anzahl und Grösse zugenommen, das Spongiosagewebe wurde stärker trabekuliert und die deformierenden Veränderungen im linken Hüftgelenk und in der Wirbelsäule wurden ausgesprochener.

Eine andere Stoffwechselstöruug, wo man mit Recht Skelettveränderungen erwarten kann, die in ihrem Aussehen mit denen bei Morbus Gaucher übereinstimmen sollen — wenn auch nicht so hochgradig — ist die Krankheit die zuerst von NIEMANN 1914 beschrieben worden ist und als Morbus Niemann bezeichnet wird. Diese Krankheit ist Morbus Gaucher sowohl klinisch wie pathologisch-anatomisch so ähnlich, dass mehrere Fälle der ersteren als »Gaucher» (BLOOM) beschrieben worden sind. Es hat sich bei der Analyse gezeigt, dass die infiltrierende Substanz bei »Niemann» ein Phosphatid ist. Der Verlauf der Krankheit ist ferner stürmischer und ihre Duration hat sich in keinem der beschriebenen Fälle über 2 Jahre erstreckt. Dies gibt ja zur Annahme Anlass, dass keine ausgedehnteren Skelettveränderungen zustande kommen sollten. Makroskopische Veränderungen des Skelettes oder Knochenmarkes sind auch nicht beschrieben, dagegen liegen Beobachtungen über typische mikroskopische Veränderungen im Knochenmark vor. Es besteht demnach die Möglichkeit für eine Infiltration in grösserer Ausdehnung ins Knochenmark, die in gleicher Weise wie bei »Gaucher» Skelettveränderungen hervorrufen kann, wie auch durch Infiltration in die spongiöse Substanz, welche Veränderungen bei der Röntgenuntersuchung zutage treten sollten.

Fig. 1.

Fig. 2.

Fig. 4.

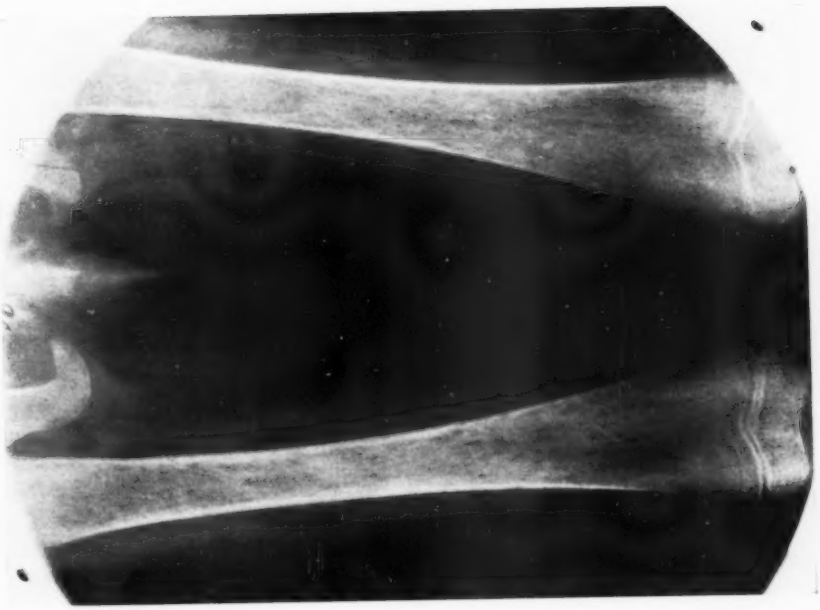

Fig. 3.

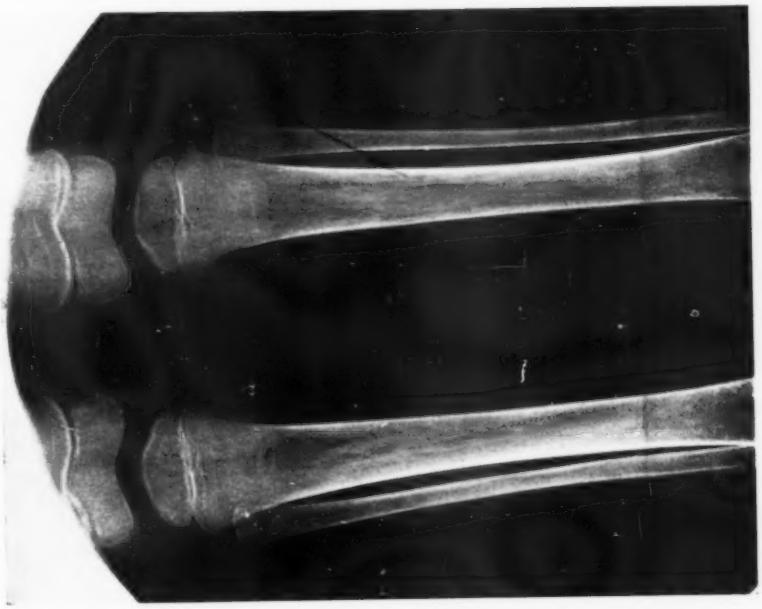

Fig. 6

Fig. 5.

Fig. 8.

Fig. 7.

Fig. 10.

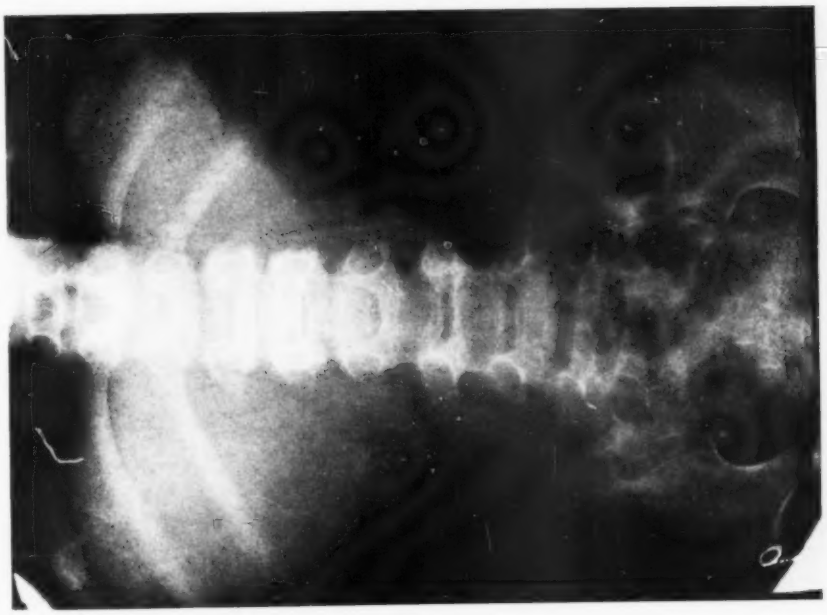

Fig. 9.

Fig. 12.

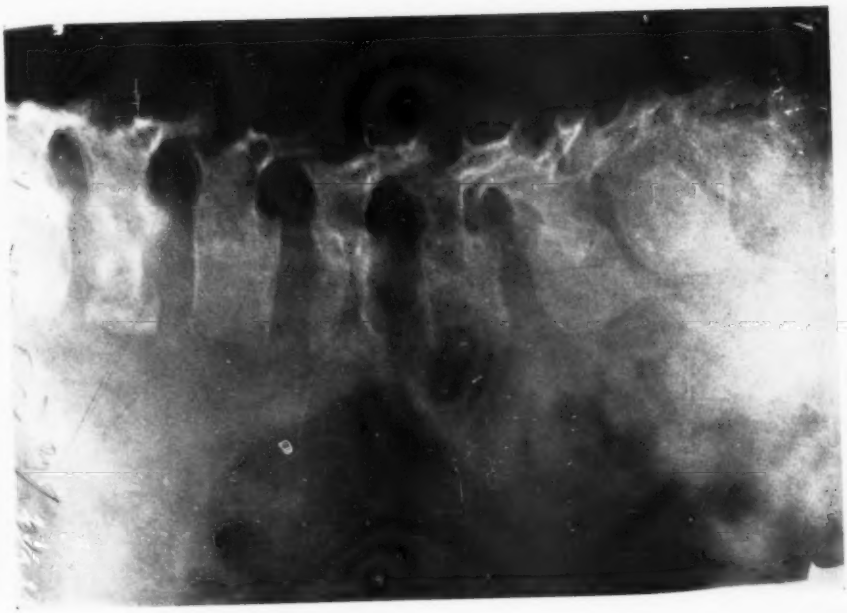

Fig. 11.

Fig. 13.

ZUSAMMENFASSUNG

Verf. berichtet über einen Fall von Morbus Gaucher, der ausgedehnte röntgenologische Skelettveränderungen aufweist. Diese geben sich zu erkennen durch

1) starke allgemeine Kalkarmut (Atrophie) im Skelette,

2) die Spongiosazeichnung erscheint grobmaschig und porös-trabekuliert,

3) Destruktion der Spongiosa, entweder in kleineren, gutbegrenzten Gebieten, wo der Knochen ein wurmstichiges Aussehen erhält, oder in grösseren Gebieten, was zu erheblichen Defekten führt, und

4) Knorpel und Periost verbleiben zum grössten Teile röntgenologisch unverändert.

SUMMARY

The author gives an account of a case of Morbus Gaucher, showing extensive röntgenological changes in the skeloton. The following are the changes that have been observed:

1) a well-marked general deficiency of calcium contents (atrophy);

2) the spongious tissue is of coarse and porous nature-trabecular;

3) destruction of spongious tissue, either in smaller well-defined areas, giving to the bone a worm-eaten appearance, or in larger areas, leading to more extensive defects;

4) cartilage and periosteum remain for the most part röntgenologically unchanged.

RÉSUMÉ

L'auteur rend compte d'un cas de maladie de Gaucher, présentant des modifications radiologiques marquées du squelette. Ces modifications se traduisent

1) par une décalcification (atrophie) marquée et généralisée du squelette;

2) par un aspect grossièrement réticulé et trabéculoporeux du tissu spongieux;

3) par la destruction du tissu spongieux, soit sur des zones restreintes et nettement délimitées au niveau desquelles l'os prend une apparence vermoulue, soit sur des zones plus étendues, ce qui conduit à des lésions graves, et

4) par l'absence générale de modifications radiologiques du cartilage et du périoste.

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FROM THE LABORATORY OF THE FINSEN INSTITUTE, COPENHAGEN
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INVESTIGATIONS CONCERNING THE PHOTOACTIVITY OF CERTAIN OILS, WITH SPECIAL REFERENCE TO THEIR EFFECT AS ANTIRACHITICS

by

Eigil Rekling

(Tabulæ XLVII—XLVIII)

Ever since HULDSCHINSKY, in 1919 and 1920, made public his researches concerning the sun and the preventive and curative effects of the ultra-violet rays in cases of rickets, investigations have been going on for the purpose of ascertaining whether those effects correspond to the ones obtained by ingestion of codliver oil — the efficacy of which, as an antirachitic, had long been known, though a closer study of it, in that respect, was not made until in 1909, by SCHABAD. That author was the first to see in the codliver oil a specific against rickets, and to show by means of biochemical experiments that ingestion of codliver oil increases the retention both of lime and of phosphorus, in individuals suffering from that disease.

HESS and UNGER, then, were the first to take up this question, which they investigated in connection with experimental rickets in rats. In 1922, they reported that they had succeeded in preventing the disease from occurring when the animals were at the same time subjected to light-baths. The discovery by IVERSEN and LENSTRUP, and by HOWLAND and CRAMER, concerning the low content of inorganic phosphorus in the blood of rachitic individuals furnished a valuable element for recognising the disease, and one which has, in fact, been made use of by American investigators. In 1923, those investigations were tested through by SONNE and SCHULTZER, who likewise found the occurrence of the rickets going hand in hand with a low figure for the phosphorus content, while the figure remained normal when the disease was prevented by means of ultra-violet irradiation — the active rays of which they found to lie between 400 $\mu\mu$ and about 280 $\mu\mu$. At the same time, the two authors took skiagrams of the bones and made microscopical investigation of the epiphyses which showed the healing process to be precisely similar

to the one obtained as the result of treatment with codliver oil. In 1923 also, PARK, POWERS and GUY measured the content, in lime and phosphorus, of blood from rats that had been put on different kinds of rickets-producing diet containing varying amounts of those two substances, and found that the figures reached normal values when codliver oil was given concurrently. In other words: they find the biochemical effect of the codliver oil, as regards the content of lime and phosphorus in the blood, to be precisely similar to the effect obtained by ultra-violet irradiation of the animals. More recently still, the problem has taken a wider scope as the result of some experimental work undertaken in America, where HESS, as well as STEENBOCK, with their respective collaborators, have succeeded in imparting to certain vegetable oils and other substances — by the means of ultra-violet irradiation — an antirachitic potency with respect to rats on a rickets-producing diet, where those same substances, non-irradiated, either did not possess that potency at all, or else in a very much slighter degree. The details of those interesting experiments cannot be gone into here, except to mention that the substances with which the investigations were undertaken were: linseed oil, cotton-seed oil, olive oil, cholesterol, phytosterol, lettuce, wheat, flour, dried milk, and spinach. In the non-saponifiable parts of the codliver oil and of the various oils that had been subjected to ultra-violet irradiation, the antirachitic potency was found to have become strongly accentuated. Subsequent to ingestion, of the substances named, after these had been subjected to irradiation, the phosphorus content in the blood of the animals thus treated was found to be considerably higher than in the rachitic animals that had been given only non-irradiated substances. HESS, WEINSTOCK and HELLMANN believe that the effect of the ultra-violet light bath must be ascribed to its action on the cholesterol contained in the skin. As HESS says: »The epidermal portion of the skin contains a large amount of cholesterol situated in its deeper layers, in close approximation to the prickle cells. It would seem quite impossible that the cholesterol in the skin is normally activated by ultra-violet irradiation and rendered antirachitic — that the solar rays and similar artificial radiations are able to bring about this conversion. This point of view regards the superficial skin as an organ which reacts to particular light waves (the epidermal organ) rather than as a mere protective covering». Similar experiments have been made, independently of the Americans, by ROSENHEIM and WEBSTER.[1]

[1] In 1912, TH. BRINCH tried to collect light-energy by irradiation of certain substances, and to use the latter for the purposes of "indirect phototherapy". He irradiated sulphate of chinine with carbon arc light and tried to cure, by means of

From all this it would seem that the codliver oil and the ultra-violet rays possess some common denominator having the quality of preventing and curing rickets. The idea then suggested itself whether that similarity of effect might possibly be due to the codliver oil emitting ultra-violet radiation. KUGELMASS and MACQUARRIE were the first to make experiments for the purpose of finding out whether the antirachitic effect of the codliver oil might be due to some such radiation from that substance. They found that the codliver oil — among other »antirachitic» substances, such as yolk of egg, bile, hydrochinone, the non-saponifiable parts of codliver oil, etc. — emitted ultra-violet rays; that is, rays that would pass through quartz, but not through glass, and which darkened a photographic plate. Oxidation of the substances heightened their effect, while reduction deprived them of their power to emit ultra-violet rays. "Non-rachitis-preventive" substances — among which the two authors count linseed oil, peanut oil, lard, glycerine, etc. — did not after oxidation darken the photographic plate through quartz, but possessed a certain amount of darkening capacity when neither glass nor quartz was interposed between the oil and the plate. The authors further found that the blood emits ultra-violet rays. They also found that irradiation by means of the mercury-quartz lamp liberates oxygen from the substances. They term that process a photolysis, and therefore believe it to be reversible. They do not state whether the ultra-violet-irradiated oils will darken the photographic plate or not.

KUGELMASS and MACQUARRIE's experiments have been repeated by SCHULTZ and MORSE, by MALMSTRÖM and by WEBSTER and HILL, but none of those investigators have been able to find any emanation of quartz-penetrating rays from the substances named. Nor does STEENBOCK find any emanation of growth-promoting ultra-violet rays from the codliver oil, in so far as the placing of quartz bottles containing that oil, in cages with rats on a diet entirely free from A-vitamines had no influence whatever on the growth of the animals. MANVILLE, on the other hand, thinks he has noticed the emanation of a bactericide radiation from the codliver oil.

In 1924, MALMSTRÖM published the results of his investigations concerning the photoactivity of sundry fatty substances following

the thus irradiated substance, animals experimentally infected with tuberculosis. Already at that time, BRINCH suggested the possibility of measuring the presence of the absorbed light rays by means of photographic plates, in the same manner in which the presence of heat rays can be measured by means of the thermometer; but he obtained no conclusive results from his experiments. Later, he experimented with letting patients suffering from tuberculosis inhale air irradiated with carbon arc light, but without notable success.

ultra-violet irradiation. Among the substances which he irradiated were: codliver oil, human fat extracted from subcutaneous tissue, cow's grease, lard, adeps lanæ, butter, margarine, cocoa butter, peanut oil, linseed oil, olive oil, colza oil, almond oil, castor oil, chaulmaugra oil, laurel oil, hyoscyamus oil, white soap, lecithin, cholesterol, human sweat, amyl alcohol, camphor, and others. He found that all of those substances, after being irradiated with light from the mercury-quartz lamp, produced a darkening of the photographic plate, but that the darkening power imparted in this manner was unable to penetrate through quartz. MALMSTRÖM sees, in the fact that blue litmus paper turns red when suspended in the air just above the surface of the irradiated oil, a proof that the latter gives off acid gases, and he believes that those gases account for the fact that a photographic plate is darkened when placed at a distance of 1 cm. from the same surface and that filter-paper can be made photographic by exposure to those »vapors». Under irradiation the acidity of the oils, as well as their darkening-power, is increased. At the same time, MALMSTRÖM made tests of numerous other substances in a similar manner, but without detecting in them any signs of their becoming photoactive; for instance: water, milk, cream, glycerin, liquid paraffin, urine, ox-bile, gelatin, casein, yolk and white of egg, sugar solution, starch, malt extract, gum arabic solution, ethyl alcohol, cloroform, quinine solution, scales cast off from the skin after photo-treatment, etc. etc. Furthermore, MALMSTRÖM found that water, when shaken together with ultra-violet-irradiated codliver oil, took up from the latter certain water-soluble constituents and became acid. This codliver-oil water possessed no plate-darkening properties, but on being boiled it gave off yellow vapors which darkened the photographic plate. Also the residium left after evaporation of the water would darken the plate. Chemical examination of the codliver-oil water — undertaken by Mr. H. PALME — revealed the presence of free acids. Quantitatively, about two thirds of these were volatile; and of those volatile acids the greater part consisted of formic acid. The non-volatile acids were found to be higher fatty acids. There were also present aldehydes and small quantities of hydrogen dioxide. With this codliver-oil water, MALMSTRÖM has instituted a therapy which he applies in cases of local tuberculosis: but with those entirely new therapeutic experiments I shall not attempt to deal here.[1]

Independently of MALMSTRÖM, HAXTHAUSEN has found that codliver oil and many fatty substances become photoactive when subjected to ultra-violet irradiation, but that this photo-action cannot exert itself

[1] At the Oto-laryngological Dep't of the Finsen Institute, the therapeutic effects of the codliver-oil water have been made the subject of investigation by S. F. NIELSEN.

through a quartz obstacle, and that the darkening of the plate is due to »vapors» — superoxides — emanating from the oils. HAXTHAUSEN has likewise examined fatty substances extracted by means of ether from the skin of patients fresh from a treatment with general light-bath, and has found that those fatty substances, too, were photo-active. He believes that the effects of the general light-bath are due to some action on the fatty substances of the skin.

It is interesting to notice that S. V. GUDJONSON has found the adeps lanæ of the iceland sheep to contain considerable quantities of A-vitamines, which he believes are excreted through the skin of those animals.

C. F. BLOCK would deny the existence of a specific antirachitic factor, but considers the energy of the ultra-violet rays to be a non-specific, activating factor which the organism can be made to receive either by direct irradiation or through certain foods — such as, for instance, codliver oil, yolk of eggs and, to a certain extent, milk — which are charged with that energy.

C. E. WALLER and J. MÖLLERSTRÖM have experimented with MALMSTRÖM's codliver-oil water and have found that its acidity increased with increased oxygenation and lengthened irradiation of the oil. As a proof that oxygen is necessary in order to obtain the photo-active effect, MÖLLERSTRÖM cites the following experiment: The »vapors» emanating from irradiated oil are drawn off by means of an air-current which has been deoxygenised through absorption of alkaline pyrogallol. This deoxygenised air is then made to pass through a glass tube containing dressing-gauze saturated with oil that has been subjected to irradiation from the mercury-quartz lamp, at a distance of 20 cm., for 45 hours. The deoxygenised air thus saturated with oil vapors is, through a tube, let into an air- and light-proof exposure-chamber containing a photographic plate. Through another tube air — or oxygen — is let into the chamber, so as likewise to act on the plate, for twenty-four hours. The result on the plates was as follows: Where the air entered there was no darkening of the plate; where the »vapors» entered a slight darkening occurred; but where the »vapors» and the air met the darkening was pronounced; that is, there existed a latent photographic agent which became activated by oxidation. Against this experiment some objections can be made, however, to which I shall come back in the following.

Independently of the investigations mentioned so far, S. HAMANO has found that cholesterol, codliver oil, butter, olive oil, oleic acid and its calcium salt, cinnamylic acid, abietic acid, camphor, borneol, menthol and other substances, became photoactive after ultra-violet irradiation. The effect observed was less pronounced in vacuum,

or in a hydrogen atmosphere, than either in the air or in an oxygen atmosphere. When the substances were inclosed in glass tubes for irradiation, only a slight effect was obtained. Neither grape-sugar, cane-sugar, starch, saturated fatty acids, succinic acid, suberic acid, amino-acids, salicylic acid, anthracene, naphtalin or cetyl alcohol, after ultra-violet irradiation, produced any effect on the photographic plate. HAMANO has subsequently shown that the same substances which became photoactive when subjected to ultra-violet irradiation also acquired that property when subjected to a very intense irradiation from the roentgen rays.

Those, as far as I know, are the most recent investigations[1] concerning the development of photographic properties in substances as the result of ultra-violet irradiation. It will perhaps be of interest to review, in this place, also the more important of the earlier researches connected with this problem.

Already before the days of photography, the influence of light on various substances had been the subject of considerable study. PLACIUS HEINRICH (1820) experimented with numerous objects — minerals, fishes, various kinds of wood, sea-weed, corals, insects, eggs, bones, horn, etc. — exposing them to the daylight for ten seconds and then examining them in a dark-room. He found that many substances after exposure to daylight became luminous in the dark, and he wrote that it was the blue end of the spectrum, especially, that possessed the property of producing that effect. »In a blue ray», he says, »a good diamond became steadily phosphorescent, while after irradiation with the red rays from the prism it remained quite dark.»

Already a short time after DAGUERRE, in 1839, had succeeded in making photographic pictures by means of a camera and an iodized silver plate, MOSER — in 1842 — began to study the action of various substances on such a »daguerroplate», and the reason for the appearance of the so-called »dew-pictures». If, for instance, a coin was placed on a polished glass- or metallic plate, and was left there for some time, was breathed upon and then removed, and the empty plate then breathed upon again, a picture of the coin would appear on the plate. It was not necessary, however, that the object should touch the plate in order to produce the phenomenon. Likewise, if he placed some object or other on the »daguerroplate», there would appear a darkening of the latter at the points where the object had been in contact with, or very close to it, when the plate was developed by means of mercury vapors. MOSER believed the production both of the »dew-pictures» and the photographic pictures to be due to some radiation emanating from the objects, and he came to the conclusion that all objects must in themselves be luminous (»dass man jeden Körper für einen selbstleuchtenden wird erklären müssen»).

Already in the same year, WAIDELE showed that the production of the »dew-pictures» was not a matter of radiation-effect, but that their appearance

[1] Quite recently, investigations have been made by H. VOLLMER concerning, the photoactivity of various vitamine-carriers, and of adrenalin. As regards the latter, he finds that its plate-darkening property is not due to any superoxide, but depends on its hydrogen-concentration.

was due to air from the coin getting over unto the glass plate from which the preceding polishing had, of course, removed the layer of air previously adhering to it, and that the change became visible only if the vapors became condensed on the plate. As regards the production of the pictures on the »daguerroplate», WAIDELE explained them as being due to a modification in the sensibility of the silver of iodide formed; a modification caused by the atmosphere emanating from the objects, as a result of which the adsorption of mercury vapors that takes place when the positive picture is developed would be different in those portions of the plate.

In 1847, NIEPCE DE SAINT VICTOR showed that the gases produced by the combustion of sulphur and phosphorus will react on the photographic plate. In 1857, he observed how a great many substances, both organic and inorganic, such as paper, chalk, marble, feathers, cotton-wool and others, by exposure to daylight acquire the property of being able to darken photosensitive paper when left in contact with the latter for twenty-four hours. The photo-action will produce itself across an air-space of up to 1 cm., and is not arrested by the interposition of a sheet of collodium or gelatin. Glass or minerals, on the other hand, will act as a bar. NIEPCE DE SAINT VICTOR believes that the effect is due to the re-emission, by the substances, of the light previously absorbed by them.

In 1896, COLSON noticed that zinc, magnesium and cadmium will darken the photographic plate, by contact or from a small distance, just as well in a vacuum as in the air. He thinks that the effect is due to the emanation of metallic vapors. He did not observe any corresponding effect from either lead, tin, copper or aluminium.

Also PELLAT, in 1896, made the photographic properties of various metals a subject of study and thinks that the effect is due to some metallic emanation. At the same time, he throws out the idea whether it might not possibly be a question of some radiation akin to that of the Becquerel rays.

The first really considerable work on the subject of photoactivity of the substances was a series of communications by RUSSELL, — for which reason the phenomenon is often termed: »the Russell effect». The publication of those communications was begun in 1897. They deal particularly with the action of metals and resinous substances on the photographic plate. RUSSELL found that especially magnesium, cadmium, zinc, nickel, aluminium, lead, bismuth, tin, cobalt and antimony possessed plate-darkening properties, and that the effect — which became stronger with increase of temperature and dampness — could pass through gelatin, rubber, celluloid and collodium, but was arrested by glass, mica and paraffin. If the metals were coated with a layer of oxidation, the photoactivity was nil. Gold, platinum and iron were never photoactive. The property could be communicated to alcohol, chloroform and water, when those liquids were left for a long time in contact with the metals. Also a current of air led over the metal became photoactive. RUSSELL likewise showed that paper, various kinds of wood (specially the resinous ones), drying oils, coal, resin, gum, turpentine and numerous ethereal oils containing terpene possess the property of darkening the photographic plate, and that their power to do so becomes enormously increased by irradiation. He furthermore found — what is interesting in this connection — that *non-irradiated codliver oil possesses the plate-darkening property in a slight degree; that it is, as he says (1898), »tolerably active»*. RUSSELL has shown that it is the blue rays in the spectrum which possess this activating power that may

last for months. As regards the cause of the plate-darkening power possessed by the substances, he believes that it is due to hydrogen peroxide, the presence of which he has proved by means of titanic acid and has thoroughly examined. He finds that, through its plate-darkening property, hydrogen peroxide can be detected in a dilution of 1 : 1,000,000, and that the degree of the darkening increases with increased concentration, temperature and duration of exposure. Very protracted »irradiation» produces solarisation of the plate. He believes the action on the latter to be of a purely chemical nature, and in support of that belief he states that the agent producing the effect does not transmit itself along straight lines, but deflects in such a manner that the »shadows» of objects that are not permeable to the action form hazy, indistinct outlines in the plate. As already stated, the photoactivity cannot exert itself through either glass, mica or aluminium, but can be transmitted to alcohol, chloroform and water. It does not disturb the electric field, cannot produce itself in carbon dioxide, but can be transmitted to inactive objects, such as paper and others.

Bela v. Lengyel (1898) believes that dampness is necessary in order to obtain the effect with zinc. According to him, the real agent responsible for it should be hydrogen set free as a result of the chemical changes taking place, in the damp atmosphere, on the surface of the zinc. In dry air the metals should be inactive. In his experience, easily oxidized gases, like carbon monoxide, ethylene and methane, produce an effect on the plate, while carbon dioxide and nitrogen do not.

Sperber (1899) would explain the action of turpentine oil on the photographic plate as the result of a molecular oscillation of the turpentine vapors, — an oscillation which should be strikingly similar to those of the ultraviolet rays.

Lewison (1900) finds that Canada balsam acts on the photographic plate, and ascribes the effect to the action of rays resembling the Becquerel rays, which can pass through black paper.

Villard (1902) has noticed that various bodies can be made photoactive by exposure to ozone. Also the ozone itself should possess the property of affecting the photographic plate, and he has observed that light-phenomena can attend the splitting of ozone.

Graetz (1902) has studied the action of hydrogen peroxide on the photographic plate and considers it to be a radiation-effect similar to that of the cathode- and Becquerel rays, because he finds that the agent responsible for it transmits itself along straight lines, is not deflected by an air-current, and passes through sheets of aluminium, as well as through false gold-leaf. He has not noticed any electric phenomena, nor any effect from ozone.

Bogojawlensky (1903) found that magnesium, aluminium, tin and zinc had a darkening effect on the photographic plate, and most strongly so when he had scraped off the oxidized layer from the metal. He believes that the action can exert itself through glass.

Oct. Dony Herault (1903) finds that ozone alone does not affect the plate, but does so only when organic substances are present; and that the photoactivity of the substances treated with ozone is due to the formation of hydrogen peroxide. The ozone acts in damp air as well, because hydrogen peroxide is formed under those conditions also.

Schaum and Braun (1904), on the contrary, show that ozone can affect pure, neutral silver bromide.

STOECKERT (1904) thinks that the action of the hydrogen peroxide is the result of ionisation, and that ozone also affects the photographic plate.

RICHARZ and SCHENK have found that sulphite of zinc becomes luminous in a current of ozone, and believe that the phenomenon should be explained as a luminosity due to oxidation, and not as an electron-radiation.

BLAAS and CZERMAK (1904) have published the results of investigations undertaken by them concerning the manner in which a variety of substances act on the photographic plate and on potassium iodamyl paper. They found that the activity was increased when the substances had previously been exposed to the rays of the sun, and all the more so the more protracted and intense that irradiation had been. Blue and violet light had the best effect. They believe that they have proved a straight-line transmission of the active agent, of which they believe that it is a radiation emanating from occluded ozone. Of paper and zinc they say that those substances »give out a radiation which belongs to the blue end of the spectrum». A sheet of red gelatin interposed will check the action, while a blue or a yellow one will not. CZERMAK also thinks he has proved a reflection of the »rays» which cannot penetrate either through metal, mica or glass. The activity can be communicated to other substances; paper. for instance, can be activated through contact with a bright zinc surface. The result of these investigations agrees with what has been shown by RICHARZ and SCHENK, but BLAAS and CZERMAK have not been able to show the existence of any visible luminosity.

STREINTZ (1904) believes that the action of metals on potassium iodamyl paper and on the photographic plate is due to emission of positive ions owing to the greater electrolytic decomposition pressure of the metals, — that of magnesium being greatest, with aluminium, zinc and cadmium next, in the order named. He determines the ionisation of the air by measuring the conductivity, and by the electrostatic method he proves an increase. S. denies the correctness of the explanation given by KAHLBAUM (see below).

MERKENS (1904) believes the action of the metals to be due to hydrogen peroxide formed in the course of their oxidation. The splitting of the hydrogen peroxide produces active oxygen which, in statu nascendi, oxidises the silver bromide into an easily reducible silver salt.

KAHLBAUM and STEFFENS (1904) observed that the metals darkened the photographic plate even without contact, and that the active agent — which they hold to be an emanation — for the most part follows the law of gravity (actinautography). Heat and dampness are important factors for bringing about the effect.

MELANDER (1905) says that all metals emit ultra-violet and violet rays as the result of certain chemical processes taking place in their surfaces. Heightened temperature increases the effect. An air-current will weaken, but not deflect, the action on the photographic plate, what MELANDER thinks would have been the case if the matter had been one of emanation.

SCHLÄPFER (1905) has investigated the photographic properties of rabbits' blood and believes them to be due to the oxygen. Normal rabbits' blood, and especially the blood of albino specimens, will darken a plate from a distance of 1 mm. and can be repeatedly activated again, by irradiation, when the photoactivity has become lost. Poisoning the blood of a rabbit with hydrocyanid acid reduced its capacity for oxidising, and the blood thus poisoned would neither influence the photographic plate, nor could it be activated by irradiation. S. believes that the effect on the plate is due to a radiation of

light from the blood owing to vital and post-vital processes of oxidation in which, probably, substanses belonging to the lecithin-group play a part. He thinks that the blood may possibly act as transmitter of the light.

PRECHT and OTSUKI (1905) come to the result that the effect of the hydrogen peroxide is not due to any radiation from the latter, but to an action of purely chemical nature. A photographic plate that has been exposed to hydrogen-peroxide vapors will, by contact, affect a fresh plate. That the active agent can pass through sheets of aluminium, they believe is due to the formation of microscopical holes in the latter, caused by the attack of the hydrogen peroxide. They have found the degree of the effect to be dependent on the temperature, and that it increases with concentration of the hydrogen peroxide up to 3 per cent, from which point it falls again at higher concentrations.

PILTSCHIKOFF (1906) thinks that some metals are positive in their action on the photographic plate, in the sense that they reduce the silver bromide; while others are negative — building up again the silver bromide reduced through action of the light; and others again merely neutral. As metals that give out positive rays he enumerates: manganese, aluminium, zinc, cadmium, tellurium, selenium, iron, cobalt, nickel, silicon, boron, phosphorus, antimony, tin, zirconium, palladium and colloidal silver; while osmium, tantalum and titanium(?) give out negative rays, and copper and brass neutral ones. The effect is increased if the air is saturated with moisture; in vacuum it is very slight. A current of air will deflect the rays; the electric or the magnetic field will not. P. believes that the effect is due to sub-atomic groups (»subatomige Gruppen»).

WERNER (1906) finds that animal tissue becomes photoactive when subjected to roentgen- or radium irradiation, and that the injection of roentgen-irradiated serum in humans or animals causes the blood of the individual thus treated to acquire photoactive properties.

ELISABETH LEGRADY (1908) says that the metals alone do not possess any photoactive properties, either in dry nitrogen, dry hydrogen or dry air. Dampness is a condition for the effect being produced, and nitrogen increases it. As to the cause of it, L. believes it to be due to the formation of ionised hydrogen, but not to hydrogen peroxide or to metallic emanations. Hydrogen alone, without metals, does not produce the effect.

DOMBROWSKY (1908) has made a critical survey of the earlier works and has made the principal experiments over again. He believes the effect of the metals on the photographic plate to be due to the formation of hydrogen peroxide.

WERMEL (1913) has found that blood becomes photoactive after roentgen-irradiation. He supposes that the roentgen rays, when absorbed into the blood, become transformed into another kind of rays, capable of influencing the photographic plate.

EDEN and PAULI (1914) have repeated WERMEL's experiments and found that non-irradiated as well as roentgen-irradiated blood possesses the photographic property. The latter is not a matter of radiation; the effect is the result of a chemical process. Electrometric investigation of non-irradiated and of roentgen-irradiated blood gave identical results as regards the movements of the electrometer.

GERLACH (1905), too, has tested WERMEL's experimental results without observing any effect on the blood from the roentgen-irradiation. Non-irradiated blood will darken the photographic plate, and the effect is due to vapors from the blood, as shown by the fact that with dried blood the effect is nil.

RUMPF (1922) has studied the photoactive properties of zinc and finds the effect to be the result of a chemical process, probably with hydrogen peroxide as the active agent. He finds that the latter passes through gelatin sheets regardless of their color. As to the fact that the active agent can exert itself through interposed aluminium sheets, he — like the earlier investigators — believes it due to microscopical holes in the latter, and he finds that the exposure has to be lengthened as the number of the sheets interposed is increased. A strong current of air would deflect the action; on the other hand, no modification of the effect resulted from putting the zinc and the plate each under a different electric tension, — what would have been the case if there had been some corpuscular radiation — ions or electrons — given out by the zinc.

In 1925, WINTHER, commenting on the Moser rays, expresses the belief that most likely hydrogen peroxide is the active agent responsible for the photoactivity of the substances. Quite another question is the manner of its action. There can hardly be any doubt but that hydrogen peroxide in the form of vapor is absorbed by the photographic plate, but as to what causes the reaction of that hydrogen peroxide upon the silver bromide is hardly known. It cannot be said for certain whether it is the result of some ultra-violet radiation (chem.: luminescence) due to the splitting of the hydrogen peroxide, but in the opinion of WINTHER there is a considerable possibility of this explanation being the true one, inasmuch as we know that a great many processes are attended with a luminous radiation, and that a great many more cause the emission of an invisible — and particularly of an ultra-violet — luminescence.

As it will be seen from all this, the interpretations of the COLSON-RUSSELL effect are widely different, being divided between radiation, ionisation, »sub-atomic groups» and chemical action. Still, it would seem that, at present, opinion is leaning toward the original conception of RUSSELL, according to which the effect of the various substances on the silver bromide plate should be due to hydrogen peroxide.

The purpose of the present contribution is to investigate whether there exists any difference between the photographic properties of the codliver oil and those of vegetable oils, in order to find, by the established proof of such a difference, a working hypothesis which would explain the spontaneous antirachitic effect of the former, as opposed to the corresponding effect of the latter, which is only acquired as a result of ultra-violet irradiation. In addition to this, the work of the author has embraced an investigation of the conditions determining the acquisition, by the ultra-violet-irradiated oils, of the photographic properties found in them; he has endeavoured to identify the nature of those properties, and he has tried to solve the question whether the antirachitic effect of those oils is really due to their photoactivity or not.

A brief description of the author's technique and of the conditions of experimentation must be given to begin with. As source of light, a mercury-quartz lamp of 2.5 ampères (160 volts) was used. The distance from the source of light to the surface of the irradiated oils was 25 cm. For irradiation and subsequent exposure with the photographic plate the oil was poured into small Petri dishes 4 cm. in diameter and 1.75 cm. high. The invariable quantity of oil used was 5 c. c., giving a distance from the surface of the oil to the photographic plate, when the latter was laid flat on the dish, of 1.5 cm. Hauff's ordinary orthochromatic plates — sensitiveness 14° Scheiner (120 HED) — were used. They were exposed with the oils for twenty-four hours, and were fastened to the dishes by means of adhesive tape. Right from the beginning of the experiments I had it in my mind to examine the »vapor» developing under irradiation. To that end I had some glass dishes made, 7 cm. in diameter, with polished rim, and fitted with glass tubes: two opposite one another, and a third one in the bottom of the dish. By means of those tubes, air or gases could be driven across the surface of the oil, or could be blown through the oil, while the latter was being irradiated. The dish was covered with a disc of quartz, about 2 mm. in thickness, which was sealed on air-tight by means of paraffin. The atmosphere, together with any »vapor» that might develop as a result of the irradiation, was drawn off through a glass tube — which, passing through a hole in a cardboard screen, was connected with one of the tubes in the dish — and could in that manner be led through various media placed back of the screen and thus protected against the rays from the mercury lamp. In those dishes, 20 c. c. was always the quantity of oil used, which gave a surface of liquid, for irradiation, of 5.5 cm., and a depth of the oil, in the middle of the dish, of 1.5 cm. When the »vapors» drawn off were led through another liquid of some kind, the quantity of that liquid worked with was in all cases 10 c. c. The drawing off was done by means of a water-suction pump. To enable us to estimate correctly the degree of change in the photographic plate, we manufactured a scale-board showing a range of 14 progressive intensities of darkening. This was made by exposing a film, at a distance of 2 metres, in front of the flame (2 cm. high) of a BUNSEN's night-burner, first for 8 seconds and then for lengths of time increasing after the quotient 1.3 for each successive exposure. The degree to which a plate had become darkened was determined by comparison with the film by observing the two simultaneously, through two openings cut in a piece of cardboard, against an illuminated white background, at the same time displacing the film until its degree of

darkness corresponded with that of the plate. The substances with which the greater part of the investigations was carried out were: codliver oil, linseed oil, as type of the drying vegetable oils; olive oil, as type of the non-drying ones; and, in some cases, peanut oil, oil of sesame, liquid paraffin, and cholesterol.

Without irradiation, codliver oil and sometimes also the other vegetable oils showed faint properties of darkening the plate. It is probable that this photoactivity depended in a certain degree on the age of the oil; for freshly extracted linseed oil[1] rarely possessed the property.

In order to find out whether there was any difference in the capacity of the oils for acquiring a certain degree of darkening power within a determined space of time, they were subjected to irradiation for periods ranging from 10 minutes to about 30 hours. After 10 minutes' irradiation the codliver oil was found to have attained a darkening-degree of 7; the others — the vegetable ones — of from 3 to 5. After irradiation for 1 hour the codliver oil had reached the degree of 11, the others that of 9 or 10. With continued irradiation it seemed as if the olive oil and the linseed oil reached the maximum of their darkening power — 12 to 13 — after from 10 to 16 hours' time, and that no higher degree was attained by them even under more intense irradiation for as much as 28 hours. To the codliver oil, on the other hand, a still stronger degree of darkening power — 14 — would be imparted by irradiation for about 24 hours; but beyond that there was no further advance in spite of irradiation continued up to, 32 hours. It will thus be seen that the codliver oil acquired a stronger darkening power more rapidly than either the olive or the linseed oil, and that altogether, under prolonged irradiation, it became more intensely photoactive than either of the two. Under irradiation, the yellow color of the codliver oil became gradually deeper as the irradiation progressed. During the first 10 hours of being under the lamp it emitted a penetrating »codliver-oil odor». After that time the odor became more like that of stearin, and from the twentieth hour onward there was no pronounced codliver-oil smell. After irradiation for 6 hours — in one case of old codliver oil after as little as 1 hour — a thin pellicle would begin to form on the surface of the oil; and this, as well as the viscosity, would grow stronger as the irradiation went on. The vegetable oils would become more and more colorless as the irradiation went on. During the earlier part of the process they would emit an odor like that of codliver oil; but

[1] Kindly furnished me by the «Danske Oljemøller», Copenhagen.

with very long irradiation that, too, became more like the smell of stearin. On the linseed oil a pellicle would form after 6 hours' irradiation. On the olive oil no pellicle would form, but under very protracted irradiation it would become of a denser consistency. Liquid paraffin could not be made photoactive by ultra-violet irradiation. Cholesterin non-irradiated possessed no plate-darkening power, but after irradiation for one hour it would darken a plate to a medium strong degree. Dissolved in purified ethyl ether and afterwards precipitated as crystals it did not become photoactive; but if the dissolving was done in ordinary technical ether the precipitated crystals would darken the plate. After irradiation for 1 hour, the cholesterin that had been treated with purified ethyl ether would produce a medium degree of darkening, similar to the result obtained with plain cholesterin after irradiation for the same length of time. In the cholesterin treated with technical ether, the plate-darkening power resulting from 1 hour's irradiation would be very strong. The residue left after evaporation of either ether had no darkening power at all, not even after being irradiated. Already in 1899 RUSSELL showed that impure ether reacts on the photographic plate, but that this power of reaction becomes lost when the ether is thoroughly purified. I have made the same observation, finding that the purified ethyl ether did not influence the plate, while the technical ether produced a slight darkening. It is curious to notice that the residue left from evaporation of the technical ether — which does not itself have any effect on the photographic plate — evidently increases the sensitiveness of the cholesterin to ultra-violet irradiation (i. e.: its photographic power).

Next, codliver oil, linseed oil (no. 221) and olive oil, in sealed quartz flasks, were irradiated. Subsequent exposure-tests with them, in the afore-mentioned small Petri dishes, showed them to have acquired no — or, at best, only the very slightest — plate-darkening power. Atmospheric air, consequently, would seem to be a condition for making them photoactive.

Inasmuch as the photoactivity of the irradiated oils is at present supposed to be due to certain «vapors» emitted by them, it lay near to investigate whether that activity could be transmitted from an irradiated oil to a non-irradiated one by subjecting the latter to the influence of vapors from the former. The disposition for that experiment was the one already described. Into a dish 20 c. c. of codliver oil was poured, and the dish, covered with a sheet of quartz, was irradiated for 1 hour with the mercury-quartz lamp, from a distance of 25 cm. During the irradiation a constant current of air was made to pass across the surface of the oil in the dish, and then

through 10 c. c. of non-irradiated codliver oil. Exposure of a photographic plate to the oil which had thus been charged with vapors from the other, irradiated oil, showed the vapor-charged oil to have become strongly photoactive (no. 59). As a control test, air, irradiated air and moist, irradiated air was forced both through codliver oil and through the vegetable oils, but none of them became photoactive as a result.

It was next tried whether it was possible to photoactivate one kind of oil with vapors from another, and it was found that this was possible with the oils that could themselves be activated by irradiation. For instance: «vapors» from irradiated codliver oil would make olive oil, linseed oil and oil of sesame photoactive; »vapors» from irradiated olive oil would photoactivate linseed oil, codliver oil and non-irradiated olive oil; »vapors» from irradiated linseed oil would have a similar effect on olive oil (no. 243), codliver oil, oil of sesame and non-irradiated linseed oil; and »vapors» from irradiated peanut oil would make oil of sesame photoactive. I tried still other variations with these oils and invariably got a positive result. By examining and comparing the degrees of darkening which the various oils were able to produce in the photographic plate after being percolated by photoactive »vapors» for a certain, given time, it was found that this degree was in every instance quite as high, at least, as what could be obtained by ultra-violet irradiation of the same oil for the same length of time. Activation of codliver oil by cholesterol was obtained after 1 hour's irradiation of the latter. Cholesterol itself could be just slightly photoactivated by exposure to »vapors» from irradiated codliver oil.

Liquid paraffin could not be rendered photoactive by the process just described. Nor did — under those conditions of experimentation — 10 c. c. of distilled water become photoactive after being percolated for 1 hour with the photoactive vapors from an irradiated oil; but on coming in contact with the plate it darkened the latter. When those vapors had passed through it, the water had become slightly yellow and acid. With a drop of chloride of iron solution it gave a brownish-violet color and a faint potassium-iodamyl reaction. It was also found that if the photoactivating vapors were made to pass through water before they were led through an oil, that oil would not become photoactive. As regards the respective capacities of the codliver oil, the linseed oil and the olive oil for giving off photoactivating vapors, it would seem to be greatest in the two former, and somewhat less in the last-named.

The next step in the investigation was for the purpose of finding how conditions would be, in the same respect, with oils that had

been irradiated for a greater length of time. To that end, thin layers of codliver oil, linseed oil and olive oil were first irradiated for about 30 hours. If, after that time, the linseed oil was irradiated for 1 hour more, and the »vapor» during that hour led through either linseed-, olive- or codliver oil, those oils would only darken a plate to a medium strong degree, and no higher degree of darkening was obtained even when the irradiation was continued for another hour and fresh portions of oil led through. When codliver oil that had already been irradiated for 28 hours was irradiated for 1 hour more, and the »vapor» during that hour led through linseed oil, a medium degree of darkening was likewise the result. But if the irradiation was continued for still another hour and, during that time, a fresh portion of either linseed- or codliver oil was passed through, a considerably stronger degree of darkening was the result. Thus, it would seem as if irradiation for an excessive length of time had caused the codliver oil to lose a portion of its capacity for giving off photoactivating »vapors» equally as powerful as those of oil that has been irradiated for only a short time.

With the excessively irradiated olive oil, matters proved different. While, as we have seen, the »vapors» of short-time-irradiated olive oil proved somewhat less photoactivating, that action increased with continued irradiation, so that 1 hour's extra irradiation of an olive oil that had already previously been irradiated for 28 hours would, when the »vapors» produced during that extra hour were led into a non-irradiated oil, make the latter capable of darkening the plate to the same degree as was obtained from linseed- or codliver oil after the first few hours' irradiation of the latter. Thus, it will be seen that the drying oils are the ones that possess the greatest power to give off photoactive vapors to a fresh oil when first irradiated, and that their power in that respect becomes less under very protracted irradiation. In the non-drying oils the same power seems to increase under irradiation for a great length of time.

Next, it was tried whether it was possible to photoactivate an oil by passing through it atmospheric air that had already been made to pass through a previously irradiated oil a few hours after that irradiation had taken place. Thus, for that purpose, 10 c. c. of codliver oil was irradiated for 1 hour (darkening degree: 11), after which time air was passed first through that and afterwards through 10 c. c. of fresh codliver oil. After that process the irradiated oil was found to give darkening-degree 7, while the fresh oil through which the air had been led gave darkening-degree 4. Linseed oil, after 1 hour's irradiation, gave d. d.: 9; after air had been led

through it for 1 hour it gave d. d.: 4; and 10 c. c. of fresh linseed oil, through which the air had subsequently passed, gave d. d.: 3. Olive oil, after 1 hour's irradiation, gave d. d.: 8; after passing of the air for 1 hour, d. d.: 5; and 10 c. c. of fresh olive oil, after the air had been led through it, d. d.: 2. Thus, it will be seen that it is possible to render oils photoactive, to a certain extent, by passing air through them which has already passed through an irradiated oil, but at the cost of the photoactivity of the latter. Now, inasmuch as it was proved that an irradiated oil could thus be made to lose a part of its photoactivity by passing air through it, it occurred to me whether it would not be possible to inactivate those oils entirely by drawing the air through them very forcibly and for a more considerable length of time. I, therefore, by means of the suction pump, forced air, for 5 hours, in a strong vacuum, through resp. codliver-, linseed- and olive oil that had previously been irradiated for 1 hour. The result was that the linseed (no. 265) and olive oil became almost completely inactivated, while the codliver oil (no. 266) had its darkening power reduced to a lesser degree and, consequently, retained its photoactivity better, — probably because the process accounting for its photographic property was considerably stronger than that in the vegetable oils. When those oils were then afterwards irradiated once more for 1 hour, they regained their original photoactivity.

The photoactivity imparted to an oil by forcing air and »vapors» through it from another oil under irradiation of the latter, could in its turn be communicated to a third oil. For instance: the »vapor» drawn off from an irradiated linseed oil was led for 1 hour through 4 glasses of olive oil, one after another. It was then found that the 1st of those portions had acquired the darkening degree 9, the 2nd portion the degree 2, while the 3rd and 4th ones did not show any darkening power at all. When ordinary air was then afterwards made to pass through those four portions of oil, in the direction from no. 1 to 4, they all became photoactive, and the degree of their darkening power was found to be, respectively: 4—4—6 and 4. In other words: portions no. 3 and 4 had become photoactive at the cost of no. 1. It was thus proved possible to transfer the photographic agent from one oil to the other. When a powerful current of air was forced, for 5 hours, through those »by perduction» photoactivated oils, they became almost completely inactivated; and this — in contrast to what was the case with the irradiated oils — was found also, and in the same degree, as regards the codliver oil. This would seem to indicate that in the oils photoactivated by the passing through of photographic vapors the process

is simply one of deposition of the active agent. Another indication pointing the same way is to be found in the fact that if (1) an oil that has been irradiated for 1 hour, and (2) an oil that has been photoactivated by »perduction» for 1 hour, are left standing for 24 hours, and a current of air is then passed through each of them and thence onward to a fresh oil, only the irradiated oil will be able to photoactivate the latter, — probably because a process is still going on in the irradiated oil.

The different capacity of the oils that have been irradiated for a great length of time (about 30 hours) to give off photoactivating »vapors» under further continued irradiation has already been spoken of. Also when air was passed through them the result was different: the air which had passed through the olive oil produced photoactivity in fresh oils, while that which had passed either through linseed- or codliver oil — a passage made very difficult, anyhow, by the increased thickening of those oils — did not. Nor could those for a long time irradiated oils — which retained their photoactivity for months — be inactivated by forcing a strong current of air through them for 5 hours.

Both the codliver oil and the vegetable oils (no. 680) can be made photoactive not only by ultra-violet irradiation and by the passage through them of photographic »vapors» from irradiated oil, but also by sending through them nitrous vapors or — as I shall come back to later — air that has passed across a hydrogen peroxide solution. Ozone, on the other hand, will have no such effect. Roentgen-irradiation, too, will make the oils photoactive, as already shown by HAMANO. After intense irradiation — with 6 Sab. through 5 mm. Al., at a focus-distance of 23 cm. — I found only a weak darkening power in linseed oil, and in codliver oil just the very slightest trace. Under ultra-violet irradiation the temperature of the oils was measured to about 34° C. Heating to that temperature or higher (140°) did not make the oils photoactive.

When non-irradiated oils were examined in regard to their photoactivity after standing for a certain length of time under free access of air, in daylight, in semi-obscurity and in complete darkness, respectively, differences were again noticed between the codliver oil and the vegetable oils. In diffuse daylight all the oils became photoactive quite rapidly; most rapidly so the codliver oil, which became resinous, and the linseed oil, on the surface of which a pellicle formed after about 1 week. When left in an almost dark room, the linseed oil was found only slightly photoactive after standing for 1 month; while the plate-darkening power of the codliver oil, under exactly similar conditions, already after two weeks was found to

be of the 5th degree, and thereafter rapidly rose to the 12th degree. Also, after standing for less than 1 month, its consistency had become quite homogeneously resinous, and it seemed to be slightly fluorescent. When left in complete darkness, the codliver oil became faintly photoactive in about two weeks and plate-darkening to the 6th degree after standing for 1 month, while the vegetable oils did not become photoactive at all in that length of time.

As regards the photoactivety of the ultra-violet-irradiated oils when left standing, the results were found to vary according to whether they had been irradiated for a shorter or longer time. Thus, when linseed- or olive oil was irradiated for 1 hour — whereby they become plate-darkening to the 9th degree — and when those oils were afterwards left to stand in a perfectly dark place, their photoactive properties were found to have practically disappeared after 2 days, but only to come back about 3 weeks later, and then increasing to such an extent that at the end of 1 month the degree of their darkening power would be higher than that of the non-irradiated oil. The codliver oil, on the other hand, loses less of its darkening power after the 2 to 4 first days, and already after two weeks it gets back its original strength equal to the one registered when exposed with the plate immediately after irradiation. It was found that the codliver oil required less additional irradiation than the vegetable oils in order to preserve its photoactive properties unreduced; and this is another proof of the fact that the same dose of ultra-violet irradiation produces a much stronger activity in the codliver oil. The oils that had become strongly photoactive either by standing or by intense ultra-violet irradiation preserved that property for many months; then, by and by, it became partly lost. Oils that after having been irradiated for 1 hour had subsequently been tapped of their photoactivity by having air forced through them for five hours, when left standing showed the same properties as those that had simply undergone the 1 hour's irradiation. With oils left standing after having been irradiated in sealed quartz flasks the results were as with the same oils non-irradiated. With oils that had been activated by having »vapors» from an irradiated oil forced through them the result was the same as when non-irradiated oils were left to stand; that is, they would lose their photographic quality after forty-eight hours, after which time they would become photoactive again with the same speed and to the same extent as non-irradiated oils under similar conditions.

If we put together these facts concerning the differences in the photoactivity of the codliver oil and the vegetable oils when left

standing, with those other facts, already demonstrated, that (1) codliver oil requires considerably less ultra-violet irradiation than the vegetable oils in order to acquire the same degree of darkening power, and (2) that the development of the photographic agent is so continuous and so intense in the codliver oil, even after only 1 hour's irradiation, that it cannot like that of linseed- and olive oil be drawn off by a current of air, then those differences in their photographic properties — which are probably the result of the drying processes going on within them — plainly show the difference between the codliver- and the vegetable oils.

The codliver oil, then, would seem to be a substance in which strong processes are going on spontaneously, and which reacts very strongly both to daylight and to ultra-violet rays, — more strongly, even, than the linseed oil, in spite of the fact that the latter's figure for Iodum lies above that of the codliver oil. It, therefore, seems to me that there was perhaps some justification for supposing that this activity in the codliver oil might be due to some light-sensitive catalyst, or sensitizer; that is, that the codliver oil was an optically sensitized substance.

It is probable, as we have just said, that the photographic properties of the oils are due to the »drying» processes; that is, to their absorption of oxygen. That air (oxygen) is necessary in order to make them photoactive was proved by the negative result of the experiments with ultra-violet irradiation of the oils in sealed quartz flasks, and will be further illustrated by the following experiments with ultra-violet irradiation in various gases.

Hydrogen[1]*:* If hydrogen, or ultra-violet-irradiated hydrogen, is made to pass through fresh linseed oil, the latter easily becomes cloudy, but there is no increase of its photoactivity. If it is irradiated in an atmosphere of hydrogen after first having been saturated as thoroughly as possible with that gas by »perduction» for 20 minutes, its photoactivity is only just slightly increased (no. 203). In a pure hydrogen atmosphere it is impossible to communicate the photographic agent to a fresh oil by sending hydrogen through it which has passed across the surface of an oil irradiated in hydrogen; but if atmospheric air, or oxygen, is for a certain time allowed to mix with the hydrogen before passing through the oil that is being irradiated there will, during that time, be created a photographic agent in such a manner that both the irradiated oil and the one through which its »vapors» are made to pass will become photo-

[1] Developed in Kipp's apparatus with pure, granulated zinc and muriatic acid. While being used, the hydrogen is led through a solution of potassium permanganate.

active. Thus, irradiation of an oil in a hydrogen atmosphere does not destroy its faculty of becoming photoactivated later on. An oil that has previously been photoactivated by ultra-violet irradiation can be almost completely inactivated by sending hydrogen through it. The same can be done with oils that have been photoactivated by the passage through them of »vapors» from irradiated oils. If, from those last-named oils, the hydrogen is led further along, through fresh oils, the latter will not become photographic; in other words: the hydrogen cannot deposit the photographic agent. If we activate an oil to a certain degree of darkening-power and then continue its irradiation in a hydrogen atmosphere, no increase in the darkening-power results. Its degree will generally remain the same; but in a few instances I have noticed that it became slightly less.

Nitrogen[1]: Nitrogen, or ultra-violet-irradiated nitrogen made to pass through linseed oil does not render the latter photoactive. Irradiation of the oil in a nitrogen atmosphere after it has previously been »saturated» with the gas produces only a slight photoactivity (no. 268); nor does a fresh oil through which the thus irradiated oil has been made to pass become photographic. But if atmospheric air, or oxygen, is allowed to mix with the nitrogen before the latter passes across the surface of the irradiated oil, then the photographic agent will be created and can afterwards be communicated to a fresh oil. If nitrogen is made to pass through an oil that has been photoactivated by means of nitrogen, that oil will become almost completely inactivated; and an oil through which nitrogen is made to pass becomes only slightly photographic. Nitrogen, consequently, possesses only to a feeble extent the power to transport a photographic agent already present. More pronounced do we find that power when the nitrogen is made to pass through oils that have been photoactivated by the passage of »vapors» from irradiated oils. In such cases the nitrogen is able to impart a medium strong photoactivity to the fresh oil. Still more plainly does the nitrogen show its power to »carry and deposit» photoactivity when oil is irradiated in the manner that thin layers of gaze is imbibed with it and suspended in front of the lamp. If the gaze is then packed losely in a glass tube — which gives a large surface for contact between the nitrogen and the oil — and nitrogen is then for several hours made to pass through a succession of such gaze-filled tubes, the oil in all of them will be made photoactive. Still, it ought to

[1] Compressed nitrogen, which during use is made to pass through alkaline pyrogallol.

be considered whether the power of the nitrogen to carry the photographic agent from one oil to another may not possibly be due to impurities, and especially to the presence of oxygen. Addition of oxygen to the nitrogen, after the latter has passed the gaze soaked with irradiated oil, does not impart any increased photographic power to the oils through which those combined gases are subsequently made to pass; while, as already mentioned, the addition of air or oxygen to the nitrogen before the latter passes through the gaze with the irradiated oil results in that oil becoming very strongly photoactive. I must, therefore, for the present remain sceptical as regards the assertion by MÖLLERSTRÖM, concerning the existence of a latent photographic agent developed by irradiation in a nitrogen atmosphere and capable of being transmitted in active form by the subsequent admission of oxygen. Nor did I come to any different result when I tried to repeat MÖLLERSTRÖM's experiment.

Carbon dioxide[1]: Neither carbon dioxide nor ultra-violet-irradiated carbon dioxide will make the oil photoactive. Linseed oil irradiated in pure carbonic acid gas after first being saturated with the same becomes only just slightly photoactive (no. 132); and to send carbon acid gas which has passed across an oil that was being irradiated through a second, fresh oil will not transfer any photographic agent to the latter. But if either atmospheric air or oxygen is allowed to mix with the gas for a certain length of time there will, during that time, be produced a photographic agent that can be transferred on to a fresh oil. Subsequent irradiation in carbonic acid gas of the oil that has previously been irradiated in the mixture of gas and atmosphere (or oxygen) leaves its darkening power unchanged. If it is once more irradiated in atmospheric air it will reach a degree of darkening power corresponding to the one that would be reached during the time it was irradiated in atmospheric air alone. Oil (linseed oil) that had previously been photoactivated by ultra-violet irradiation could be almost completely inactivated by sending carbon acid gas through it, and the same could be done with oils that had been photoactivated by the passage through them of »vapors» from irradiated oils. No more than the hydrogen could the pure carbon acid gas carry the photographic agent and deposit it in a fresh oil. The following extract from the Journal of experiments will give a clear idea of the results come to:

[1] Compressed carbon dioxide.

No. 519 — linseed oil — irrad. 30 min. — degree of darkening power 7
» 520 — » » — irrad. 30 min. + irr. in c. a. gas 1 hour — degree of darkening power 7
» 521 — » » — irrad. 30 min. + irr. in c. a. gas 1 hour + irr. in air 1 hour — degree of dark. power . . *10*
» 514 — » » — air from 519 sent through for 30 min. — degree of darkening power *8*
» 516 — » » — c. a. gas from 520 sent through for 1 hour — degree of darkening power *0*
» 518 — » » — air from 521 sent through for 1 hour — degree of darkening power *8*

Oxygen[1]: Oxygen, or ultra-violet-irradiated oxygen, made to pass through an oil does not make the latter photoactive. Irradiation of the oil in a pure oxygen atmosphere after oxygen has previously been sent through it for about 30 minutes usually gives it a degree of darkening power similar to what would be obtained by ultra-violet irradiation in ordinary air. In a few instances the oil became only slightly photoactive. If atmospheric air is added to the oxygen a strong photoactivity is obtained, and the same is the case if the irradiation is undertaken first in atmospheric air and subsequently continued in oxygen. From this it would seem that there exists an optimum for the concentration of the oxygen, at which it possesses its greatest power to set going that process in the oils which determines the development of the photographic agent. If this optimum is exceeded the photoactivity becomes less. On the other hand, irradiation in pure oxygen seems to be an excellent promoter of the process when the latter has first become started through irradiation in atmospheric air. As already stated, the same degree of photoactivity can generally be obtained by ultra-violet irradiation of the oils in a pure oxygen atmosphere as by their irradiation in ordinary air, even after they have been thoroughly saturated with oxygen. In a few instances the photoactivity registered under exactly those same conditions was only insignificant (no. 476). That is a phenomenon for which I am unable to find any explanation. I do not know whether, possibly, it is the air adsorbed by the oils that plays the part of the capricious factor; anyhow, vacuum treatment of them for 5 hours previous to their being saturated with the oxygen and irradiated in an atmosphere of the latter failed to remove that element of capriciousness. Another circumstance which ought perhaps to be taken into consideration also is the formation of ozone, because pure ozone absorbs practically all rays from 300 $\mu\mu$ outwards. This linseed oil which by irradiation in oxygen only became slightly

[1] Compressed oxygen.

photoactive did not, as was the case with the others, become paler; on the contrary, it turned an intense yellow, its smell became stronger, and it seemed to me that it did not become quite as viscid. Even when left standing for several months in daylight it did not draw any skin, and there was practically no increase in its photoactivity. Thus, it would seem that this linseed oil had to a great extent lost its ordinary drying qualities.

When oxygen is made to pass through an oil while the latter is itself being irradiated in oxygen, and is thence made to pass into a fresh oil, that second oil invariably becomes photoactive, and the degree of that photoactivity will be about the same regardless of whether the irradiated oil was strongly photoactive or not. The addition of atmospheric air to the oxygen in which the first-named oil is irradiated will, as already stated, increase its photoactivity; but also the second oil — the one through which oxygen is sent after having passed through the former — will have its photoactivity increased in consequence. Oxygen that is made to pass through an oil that has beforehand been made photoactive by irradiation will carry along the photographic agent and by depositing it activate a fresh oil, in the same degree as would the atmospheric air. So will the oxygen that has been made to pass through an oil made photoactive by means of photoactive »vapors»; but in either case at the cost of a reduction in the photoactivity of the — respectively irradiation- and »vapor»-activated — oil. Just as successive portions of fresh oil can be activated by sending through them a current of atmospheric air that has first passed through an irradiated oil, so can this be done in the same way by sending a current of oxygen through them under the same conditions. Oils that have been left standing for a length of time after being irradiated for 1 hour in an oxygen atmosphere, or after having had oxygen sent through them, develop the same characteristics as those which have been treated with atmospheric air in a similar manner.

We have thus seen that neither in a hydrogen-, a nitrogen- or a carbon dioxide atmosphere will ultra-violet irradiation make the oils photoactive, or, at any rate, it will make them only very slightly so; while irradiation in oxygen will, as a rule, produce the same effect as irradiation in atmospheric air and only in quite exceptional instances causes such complete changes in the oil as the ones just described. The sending of oxygen through oils while these are being irradiated in hydrogen, nitrogen or carbon dioxide, has the same effect as the sending through them of atmospheric air under the same conditions; namely, of making them photoactive.

It might now be imagined that the complete, or almost complete,

failure of the oils to develop photographic properties under irradiation in an atmosphere of any of the three gases named was due to absorption, in those gases, of the ultra-violet portion of the spectrum, of which we know that it has a catalytic effect as regards the drying processes. In order to test this, I constructed a sort of air-chamber on top of the quartz plate covering the dish with the oil. This chamber was formed of a glass ring, 25 mm. high and of the same diameter as the dish underneath, sealed by means of paraffin to the quartz plate on which it reposed and covered by a second plate of quartz, likewise sealed on air-tight by means of paraffin. Two tubes leading out from the ring permitted admission and exhaustion of gas to and from the chamber. I thus had a receptacle comprising two compartments, each with its tubes for admission and exhaustion of gas or air. The lower one of these contained the oil with the atmospheric air, the upper one the gas. Under those conditions it was found that neither hydrogen, nitrogen or carbon dioxide had any influence on the creation of photoactivity in the oils, and that the photoactivity created could be carried on and deposited in a fresh oil by the current of air allowed to pass from one oil to the other. Ultra-violet irradiation through oxygen filter seemed to lower the intensity of the photographic processes somewhat. This accords with the spectra of the hydrogen, the nitrogen and the carbon dioxide, as well as with that of the oxygen, which, neither of them, show any absorption to speak of except from about 180 $\mu\mu$ outward. Ozone, on the contrary, absorbs one tenth of the rays already at 310 $\mu\mu$, and practically all of them from 295 $\mu\mu$ outward. As regards irradiation in an oxygen atmosphere it is, therefore, necessary to count with the possibility that a formation of ozone may be the reason why part of the active rays disappear.

Comparative Tests with Hydrogen Peroxide and the Photographic Agent Developed in Oils by Ultra-Violet Irradiation

In the first part of this communication — the historical notes — I described how the photographic qualities discovered both in irradiated and in non-irradiated substances are at present believed to be due to hydrogen peroxide — a theory already advanced by RUSSELL. It, therefore, lay very near to examine whether there was anything to oppose the acceptance of the effect of the oils on the photographic plate as really due to an action of that character. My next experiments, consequently, were for the purpose of finding out whether those photographic »vapors» emanating from hydrogen peroxide were capable of activating the oils. To that end, a current of air was

made to pass across a 3 per cent. solution of hydrogen peroxide and then through linseed oil. The latter immediately became strongly photoactive. When a strong current of air was afterwards sent through the same oil for 2 hours it became almost completely inactivated, just as was the case with oils that had been photoactivated by sending »vapors» from irradiated oils through them. Hydrogen peroxide in 3 per cent. solution is strongly photographic. The same is the case with its higher dilutions. Thus, in solution of 1: 1000 it produced a darkening of the photographic plate similar to what was obtained by exposure of the latter for 24 hours to linseed oil that had been irradiated for 1 hour. When air was made to pass first through this weak hydrogen peroxide solution and then afterwards through fresh linseed oil, the latter became photoactive to the same degree as it would have become by the passage through it of air that had first for 1 hour passed through »1-hour-irradiated» linseed oil. When air that had passed through a 1: 1000 solution of hydrogen peroxide was made to pass through 10 c. c. of water, the latter would darken the plate only when coming in contact with it, — just as was the case with water through which »vapors» from irradiated oils had been made to pass. Liquid paraffin could not be photoactivated by means of hydrogen peroxide vapors.

The next step was to investigate whether hydrogen peroxide and the photographic agent manifest in the oils acted alike under the various circumstances and conditions that by earlier writers on the subject have been used to support the theory that the phenomenon was due to an action of hydrogen peroxide. The action of the hydrogen peroxide cannot exert itself through either glass, quartz, mica or paraffin, all of which substances, consequently, produced a »screening-effect» in the photographic plate. The »shadows» of their outlines appear in the plate indistinct, washed-out, and increasingly so the more the distance from the »screen» to the plate is increased; in other words: the photographic agent diffuses itself in between the »screen» and the plate. Precisely the same was found to be the case with the photographic action emanating from the oils. Paper or thin sheets of either collodium or gelatin form no obstruction to the action of the hydrogen peroxide, no more than to that of the photographic agent present in the oils that have been activated either by irradiation or by having photoactive »vapors» sent through them. If we expose two photographic plates to the action of the hydrogen peroxide for some hours and then develop one of them immediately afterwards, while the other is left lying, well protected against the light, for 24 hours, before being developed, then the second of those two plates will show a considerably stronger degree of

darkening; or, in other words: an »after-ripening» of the plate has taken place. DOMBROWSKY, who has been the first to try to explain this, expresses the opinion that the action of the hydrogen peroxide on the plate takes place in two tempi: a rapid adsorption, and a slow reaction of the silver bromide. The same experiment made with the oils gives an exactly similar result.

If we expose a plate for some hours to the action of the hydrogen peroxide and then immediately place a fresh plate on top of it and let them lie together for 24 hours, a latent picture will at the end of that time have formed on that second plate also. But if we let the first plate lie for 48 hours before placing it together with the fresh plate no latent impression will be made on the second one, which proves that the reaction between the hydrogen peroxide and the silver bromide of the first plate has by that time been fully terminated and there no longer remains any free hydrogen peroxide that might influence the second plate. The observations made with oil-effects under similar circumstances were precisely the same.

I shall mention still some other points of similarity between the hydrogen peroxide and the photographic agent present in the oils. A solution of potassium iodide weakens the »oil picture» precisely as it weakens the »peroxide picture». If a filter-paper saturated with potassium iodide is interposed between the irradiated oil and the photographic plate the oil will make no impression on the latter, and the potassium iodide paper will turn brown. If we rub the filter-paper all over with precipitated manganese dioxide, which splits up the hydrogen peroxide, the latter will make no impression either, on the plate, even after exposure for 48 hours. But if instead of the manganese dioxide we use some other black substance, indifferent toward hydrogen peroxide, the effect on the plate will be produced. An analogous observation will be made if precipitated manganese dioxide is deposited in the photographic oil. If during the exposure of the plate for 24 hours with a photoactive oil a strong current of air is made to pass across the latter it will be found that the resulting darkening of the plate is uneven (no. 655), because the air-current has carried the photographic agent along with it, so that those portions of the plate in the neighbourhood of which the current has been strongest have not been darkened as much as others. The plate-darkening agent which can, thus, be driven along with the current of air would seem to be identical, then, with the one that can be deposited in the oils. Electrometric tests[1] failed to reveal any power of ionisation in the oils.

[1] Kindly undertaken for me, with an alpha-electroscope, by Mr. EBBE RASMUSSEN, M. A.

It has now been shown that hydrogen peroxide and the photographic agent present in certain oils possess the same properties and produce the same results in the following respects:

1. Penetration-power, resp. lack of that power, as regards a variety of media (»screen-effect» of the latter).
2. Carrying off of the photographic agent by a current of air.
3. Ionisation.
4. Destructive effect on the photographic power, of substances capable of splitting up hydrogen peroxide.
5. Photoactivity of the plate in regard to fresh plates, and »after-ripening» of the plate.

It now remains to see whether it is possible to demonstrate the presence of hydrogen peroxide in the photographic agent manifest in the oils. There exist numerous reagents for hydrogen peroxide, but I have used only those of SCHOENBEIN (potassium iodamyl and sulphate of iron) and of RICHARDSON (titanic acid). With the former, even nonirradiated oil gave a weak reaction after a while; but of the photoactive oils the reaction was both stronger and more rapid, regardless of whether their photoactivity was the result of irradiation or of »vapors» from an irradiated oil being sent through them. A comparison between those reactions and the ones produced in solutions of hydrogen peroxide showed that the latter remained steadily blue, while the oil reactions turned from blue to various tints of violet. If, however, an oil was made photoactive by having hydrogen peroxide vapors sent through it, its reaction to the potassium iodamyl and sulphate of iron was precisely like that of the irradiated oils. Also the photographic »vapors» emanating from the latter reacted when made to pass either through the reagent itself or up against a piece of filter-paper saturated with it. SCHOENBEIN's reaction is not a specific hydrogen-peroxide test, but reacts with ozone and nitrous acid as well. It was, therefore, tested whether the oils gave specific ozone reaction. For that purpose, ERLWEIN's reagent (metaphenyldiaminchlorohydride) — which is stated not to react with hydrogen peroxide — was used, as well as »ozone paper» (benzidine) which is less specific. With both of these the oils gave positive reaction, most so the resinous oils. The »vapors» from irradiated oils gave reaction with RICHARDSON's reagent when made to pass through the latter. Also the oils themselves gave positive reaction after being shaken and left to stand with this reagent, which is held to be specific.

It was stated in the foregoing that an oil can be made photoactive by having nitrous acid gas or nitrous vapors sent through it.

Those gases do not give any reaction with titanic acid, but it is well known that they react strongly with potassium iodamyl and sulphate of iron, as well as with ERLWEIN's reagent and with the »ozone paper», which turns a greenish blue. An oil through which those nitrous gases had been made to pass likewise reacted strongly on the reagents here named. The ozone paper turned a reddish brown, and the quality of the potassium iodamyl-sulphate-of-iron reaction was found to resemble those of the irradiated oils, being of a violet color.

Still another experiment showing the resemblance of these gases and the hydrogen-peroxide effect to the photographic agent resident in the oils is as follows: A photographic plate that has been exposed to photoactivated oil for 24 hours is afterwards exposed to the daylight. After a very short while there will be noticed in it a darkening corresponding to that part of the surface which had been exposed to the photographic »vapors». When still left exposed to the daylight the rest of the plate will gradually darken in the usual way, so that the contrast between the vapor-exposed portion and its surroundings will become more or less effaced; but nevertheless the former will continue to be visibly darker than the rest. If, now, we repeat this experiment using a plate that has been exposed to an oil through which either nitrous or hydrogen peroxide vapors have been made to pass we shall find that the result is exactly the same as with the first one. With a plate that has been exposed to the hydrogen peroxide solution directly a somewhat different result is noticed. Here the exposed portion of the plate retains its original color for a while and seems more transparent than the surrounding area, which under the influence of the daylight changes in the normal way. Gradually, however, the exposed portion begins to darken also, and finally ends by becoming darker than its surroundings.

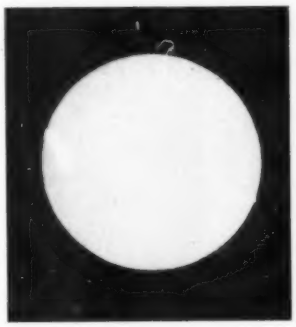
Thus, there is very much to indicate that the photographic agent present in the oils is not a radiation, is not due to ionisation, but is in all probability a »Russell effect»; or, in other words, that it is due to hydrogen peroxide set free as a result of the oxidation of the oils. Nor is it beyond possibility that nitrous oxides — which, according to FAHRION, occur in connection with the formation of ozone that attends the drying processes in the oils — may have something to do with its creation.

With the question of the connection between the photographic properties of ultra-violet-irradiated oils and the antirachitic potency of the latter I intend to deal in a following article, and I shall, therefore, only just touch on it here. Neither by giving

rats on a rickets-producing diet a daily dose of linseed oil photoactivated by deposition of photographic emanations from ultra-violet-irradiated oils, nor by keeping the animals constantly exposed to the photographic agent by having their cages placed over dishes filled with ultra-violet-irradiated oil, was any antirachitic effect ever obtained. When the photographic agent was removed from an ultra-violet-irradiated linseed oil by passing air through it, that oil nevertheless retained its antirachitic potency. When the oils were irradiated without admission of the air they became antirachitic in spite of the utter slightness of the photographic properties developed. The same, according to HESS, is the case when the irradiation takes place in a nitrogen atmosphere. When linseed oil has been irradiated for a very great length of time (30 hours) it no longer has any antirachitic potency, but it will have become strongly photographic. According to STEENBOCK, olive- and codliver oil that has been irradiated for from 10 to 17 hours no longer possess any calcifying or growth-promoting properties, while we know that they still remain strongly photoactive. Roentgen-irradiation (6 Sab. through 5 mm. al.) made the linseed oil photoactive to a medium degree, but did not give it any antirachitic potency.

Oils through which hydrogen peroxide vapors had been made to pass did not, in spite of being strongly photoactive, possess any antirachitic potency; nor did hydrogen peroxide alone — a fact which has already been pointed out by HESS. To send nitrous vapors through an oil makes it strongly photoactive but does not give it any antirachitic qualities either; on the contrary, according to BILLS, the nitrous gases should be able to destroy the antirachitic principle in codliver oil. From all this it is evident that the antirachitic potency of the ultra-violet-irradiated oils does not depend on the photographic agent called to life by the irradiation, nor does it depend on the drying processes themselves.

If, now, we would try to draw a parallel between the antirachitic properties of the ultra-violet rays and those of the codliver oil we must first of all consider the views expressed by HESS and HAXTHAUSEN. The ultra-violet rays determine a process in the cholesterol of the epidermis, or in the fatty substances of the skin, whereby the latter become antirachitic (i. e. they activate those substances), or processes are set going which result in the formation of antirachitic products. I believe that the codliver oil must be considered as a substance in which, thanks to some light-sensitive catalyzer (or sensitizer), the ordinary daylight sets going processes similar to those which the ultra-violet rays set going in the fatty substances, resulting in the formation of products possessing antirachitic potency.



No. 59. Codliver oil photoactivated by having sent through it »vapors» from another codliver oil during the latter's irradiation for 1 hour.

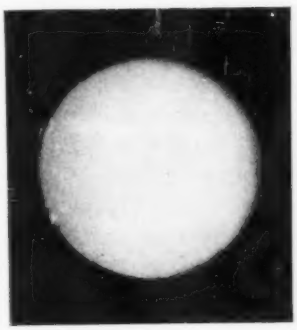
No. 132. Linseed oil after ultraviolet irradiation for 1 hour in a carbon dioxide atmosphere.

No. 203. Linseed oil after ultraviolet irradiation for 1 hour in a hydrogen atmosphere.

No. 221. Linseed oil after ultraviolet irradiation for 1 hour in a quartz flask with no admission of air.

No. 243. Olive oil photoactivated by having sent through it »vapors» from linseed oil during irradiation of the latter for 1 hour.

No. 265. Linseed oil after 1 hour's ultra-violet irradiation and subsequent passage through it of atmospheric air for 5 hours.



No. 266. Codliver oil after 1 hour's ultra-violet irradiation and subsequent passage through it of atmospheric air for 5 hours.

No. 268. Linseed oil after ultra-violet irradiation for 1 hour in a nitrogen atmosphere.

No. 476. Linseed oil after ultra-violet irradiation for 1 hour in an oxygen atmosphere.

No. 655. During exposure to a photoactive oil for 24 hours a current of air has been made to pass across the film of the plate. It can be plainly seen how the photographic agent has been carried along by the air-current. The arrow indicates the direction of the latter.

No. 680. Linseed oil photoactivated by the passage through it of nitrous vapors.

With its content of a sensitizer, or light-sensitive catalyst, the cod-liver oil, then, is an optically sensitized substance, by the ingestion of which the organism receives not only the antirachitic products but also the »catalyzer», which makes it sensitive to the light. An important question, therefore, presents itself: Does the lack, or absence, of a sensitizer or light-sensitive catalyst have anything to do with the origin of rickets in an organism? As a result of the discovery, by HAUSMANN and SONNE, that the hematoporphyrin has a sensitizing effect as regards certain parts of the ultra-violet field of the spectrum, the further question presents itself whether this kind of sensitization may not be a far more general thing than hitherto supposed, and whether it may not, possibly, play a part in connection with the pathogenesis of rickets, seeing that it is precisely certain groups of ultra-violet rays that have a curative and preventive effect as regards that disease.

SUMMARY

Comparative investigation concerning the photoactivity of respectively codliver-, linseed- and olive oil shows that the first-named, in contrast to the two others, always impresses the photographic plate. Also that codliver oil, when left to stand for a certain length of time in complete darkness or in semi-obscurity, develops a respectively medium-strong and very intense plate-darkening power, while under similar conditions the linseed oil develops respectively none or only a very slight one, and the olive oil does not become photoactive at all. Ultra-violet irradiation, under identical conditions of dose and distance, of the three oils in identical quantities and presenting the same extent of surface, produces a much stronger photoactivity in the codliver oil than in any of the two others. From the vegetable oils the photographic agent can again be removed completely by forcing air through the oil; from the codliver oil the same process will only remove it partially. If the ultra-violet irradiation has been lengthy, the air-forcing process will not destroy the photoactivity. Codliver oil demands less additional ultra-violet irradiation in order to retain its full amount of photoactivity. Ultra-violet irradiation in an atmosphere of either N_2, CO_2 or H_2 will not make the oils photoactive, or at least only slightly so. The presence of oxygen during the irradiation is a necessary condition for the genesis of photoactivity in the oils. The photographic agent can be transferred to a fresh oil from an already photoactive one by having a current of air from the latter pass through it. The fresh oil will then become photoactive in its turn, and will resemble H_2O_2 1) in its ability to react photographically through paper and through membranes of either collodium or gelatin, but not through either glass, quartz, mica or paraffin; 2) in the fact that there takes place an »after-ripening» of the plate that has been exposed to the photo-agent present in the oil and that, within certain limits of time, that plate itself will possess a degree of photoactivity in regard to fresh plates; and 3) in the fact that substances capable of splitting up hydrogen peroxide will have a destructive effect on the photographic agent. There is no ionisation in connection with the photo-

activity of the oils. The presence of H_2O_2 has been proved by means of SCHOENBEIN's and RICHARDSON's reactions. The photoactivity of the substances in question must, under those circumstances, be taken to be due chiefly to the formation of this H_2O_2, in the oils, in the course of the oxidative (drying) processes in the latter; and, furthermore, the oils can be photoactivated by the process of sending through them air that has been made to pass across an H_2O_2 solution. — Experiments undertaken with rats on a rickets-producing diet did not reveal any seeming parallelism between the photoactivity and antirachitic potency in the oils. If we use the photoactivity of the oils as an indicator for measuring the degree of their reaction to those factors — ultra-violet irradiation and daylight — that catalyze the drying processes, it would seem that the codliver oil is a substance which is in continual, strong activity, and which reacts to those factors far more easily than does either linseed- or olive oil. It lies near, then, to suppose that the codliver oil contains some light-sensitive catalyzer or photodynamic substance in which also ordinary daylight more easily sets going antirachitic processes, and that the lack of some such optical sensitizer may possibly account for the genesis of rickets in the organism of the child.

ZUSAMMENFASSUNG

Vergleichende Untersuchung der Photoaktivität von Lebertran-, Leinsamen- und Olivenöl zeigt, dass das erstgenannte im Gegensatz zu den zwei anderen immer eine Einwirkung auf die photographische Platte hat. Ferner dass Lebertran, wenn er eine gewisse Zeit in völlig dunkelm oder halbdunkelm Raum stehen gelassen wird, eine mittelstarke oder sehr intensive plattenschwärzende Fähigkeit erlangt, während sich beim Leinsamenöl unter ähnlichen Bedingungen eine solche gar nicht oder nur sehr schwach entwickelt und das Olivenöl überhaupt nicht photoaktiv wird. Ultraviolette Bestrahlung von gleichen Mengen und von gleich grossem Oberflächenausmass der drei Öle erzeugt im Lebertran eine viel stärkere Photoaktivität als in den beiden anderen. Aus den vegetabilischen Ölen lässt sich das photographisch wirksame Agens wieder vollständig entfernen, indem man Luft durch das Öl presst; aus dem Lebertran kann derselbe Prozess sie nur teilweise entfernen. Wenn die ultraviolette Bestrahlung von längerer Dauer war, ist die Photoaktivität durch den Durchlüftungsprozess nicht zu zerstören. Lebertran erfordert weniger nachträglich ergänzende ultraviolette Bestrahlung, um seine volle Stärke von Photoaktivität zu bewahren. In einer Atmosphäre von N_2, CO_2 oder H_2 macht die ultraviolette Bestrahlung die Öle nicht photoaktiv oder wenigstens nur sehr schwach. Die Gegenwart von Sauerstoff während der Bestrahlung ist eine notwendige Bedingung für die Entstehung der Photoaktivität der Öle. Das photographische Agens kann aus einem bereits photoaktiven Öl auf frisches Öl übertragen werden, indem man einen Luftstrom durch das erstere in das frische gehen lässt. Das frische Öl wird dann seinerseits photoaktiv und dem H_2O_2 ähnlich werden, 1) insofern als es imstande ist, durch Papier oder durch Membranen von Kollodium oder Gelatine photographisch zu wirken, aber nicht durch Glas, Quarz, Glimmer oder Paraffin, 2) darin, dass eine »Nachreifung« der Platte eintritt, die dem im Öl vorhandenen Photo-Agens ausgesetzt war, und dass innerhalb gewisser Zeitgrenzen die Platte selbst frischen Platten gegenüber einen Grad von Photoaktivität

besitzen wird, 3) darin, dass Substanzen, welche Wasserstoffsuperoxyd zu spalten vermögen, einen zerstörenden Einfluss auf das photographische Agens haben. Eine Ionisation besteht in Verbindung mit der Photoaktivität der Öle nicht. Die Gegenwart von H_2O_2 ist mittels der Reaktionen von SCHOENBEIN und RICHARDSON nachgewiesen worden. Unter diesen Umständen muss man annehmen, dass die Photoaktivität der in Rede stehenden Substanzen hauptsächlich auf diesem H_2O_2 beruht, das sich in den Ölen im Laufe des oxydativen (Trocknungs-)Prozesses bildet; auch können die Öle photoaktiviert werden, indem man Luft durch sie durchsendet, die man erst durch eine H_2O_2-Lösung geleitet hat. Experimente an Ratten, die auf einer rachitiserzeugenden Diät standen, liess keinen merklichen Parallelismus zwischen Photoaktivität und antirachitischem Vermögen der Öle erkennen. Wenn wir die Photoaktivität der Öle als Indikator für das Messen des Grades ihrer Reaktion auf diejenigen Faktoren benützen, welche die Trocknungsprozesse katalysieren — ultraviolette Bestrahlung und Tageslicht —, so erhält man den Eindruck, dass Lebertran eine Substanz ist, die sich in kontinuierlicher starker Aktivität befindet und welche auf die erwähnten Faktoren weit leichter reagiert als Leinsamen- oder Olivenöl. Es liegt also die Vermutung nahe, dass Lebertran einen lichtempfindlichen Katalysator oder eine photodynamische Substanz enthält, in der auch das gewöhnliche Tageslicht leichter antirachitische Prozesse in Gang setzt, und dass der Genese der Rachitis im Organismus des Kindes vielleicht ein Mangel eines solchen optischen Sensibilisators zugrundeliegt.

RÉSUMÉ

De recherches comparatives effectuées sur la photoactivité de l'huile de foie de morrue, de l'huile de lin et de l'huile d'olive, il résulte que seule la première, au contraire des deux autres impressionne dans tous les cas la plaque photographique. On a constaté également que, laissée pendant un certain temps dans l'obscurité complète ou dans une demi-obscurité, l'huile de foie de morrue développe un pouvoir noircisseur de la plaque photographique d'intensité moyenne dans le premier cas et très intense dans le second, tandis que dans les mêmes conditions, l'huile de lin n'acquiert qu'une action respectivement faible ou nulle et l'huile d'olive reste sans action photo-active. L'irradiation ultra-violette pratiquée dans des conditions identiques de dose et de distance sur une quantité et une surface identiques de ces trois genres d'huiles détermine une photo activité bien plus intense pour l'huile de foie de morrue que pour les deux autres. Les huiles végétales peuvent être débarrassées de l'agent photogénique par le barbottage d'air à travers elles; ce même procédé appliqué à l'huile de foie de morrue ne détermine qu'une disparition partielle de cet agent. Si l'irradiation ultraviolette a été suffisamment prolongée, le barbottage d'air reste sans action sur l'agent photogénique. L'huile de foie de morrue exige, pour garder son plein pouvoir photogénique, une moindre quantité d'irradiations ultra-violettes supplémentaires. Dans une atmosphère de N_2, de CO_2 ou de H_2, l'irradiation ultra-violette ne rend pas l'huile photo-active, ou ne la rend photo-active que dans de faibles proportions. La présence d'oxygène pendant l'irradiation est une condition nécessaire pour

que l'huile devienne photo-active. L'agent photogénique peut être transmis d'une huile déjà photo-active à une huile fraîche en faisant simplement passer un courant d'air de la première dans la seconde. L'huile fraîche devient à son tour photo-active et acquiert avec l'eau oxygénée les propriétés communes suivantes: 1. possibilité de déterminer une réaction photographique à travers le papier ou à travers des pellicules de collodion ou de gélatine, mais non à travers le verre, le quartz, le mica ou la paraffine; 2. la production d'une sorte de »post-maturation» de la plaque exposée à l'agent photogénique contenu dans l'huile et la propriété acquise par la plaque, dans certaines limites de temps, de devenir elle-même et à un degré déterminé photoactive vis-à-vis d'autres plaques fraîches; 3. destruction, par l'action de corps susceptibles de décomposer l'eau oxygénée de l'agent photogénique. Cette photoactivité de l'huile n'a aucun rapport avec des phénomènes d'ionisation. La présence d'eau oxygénée a été établie à l'aide des réactions de SCHOENBEIN et de RICHARDSON. Dans ces conditions, la photoactivité des substances en question doit être considérée comme due avant tout à la formation de H_2O_2 dans l'huile, par suite d'un processus d'oxydation (déshydratation) qui se passe au sein de celle-ci; de plus, l'huile peut être rendue photo-active, par le barbottage d'un courant d'air ayant préalablement traversé une solution de H_2O_2. Des expériences effectuées sur des rats soumis à un régime rachitogène ne révèlent aucun parallélisme manifeste entre la photo-activité et le pouvoir antirachitique des huiles. Si l'on considère la photo-activité des huiles comme l'index de l'intensité de leur réaction vis-à-vis des facteurs — irradiations ultra-violettes et lumière solaire — catalysateurs du processus de déshydratation, il semble que l'huile de foie de morrue constitue une corps en état d'activité permanente et intense, et réagissant à l'égard de ces facteurs d'une façon bien plus marquée que l'huile de lin ou l'huile d'olive. Il paraît donc vraisemblable que l'huile de foie de morrue renferme certains catalysateurs photo-sensibles ou un corps photodynamique au sein duquel la lumière solaire ordinaire déclenche également avec plus de facilité le processus anti-rachitique et que l'absence de ce corps photo-sensible explique la genèse du rachitisme dans l'organisme de l'enfant.

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FROM THE STATE INSTITUTE FOR THE STUDY OF MALIGNANT DISEASE, BUFFALO, NEW YORK
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SOME MEASUREMENTS OF THE TRANSPARANCY OF SKIN TO LIGHT

by

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Few quantitative measurements have been made to establish how much of the light striking the skin penetrates it. We, therefore, undertook the following experiments as a contribution to the solution of this problem.

If a beam of light strikes the skin under normal incidence, part of the radiation is reflected, part is absorbed, part goes straight through and part is scattered in all directions. It is evident that a considerable part of the scattered radiation also penetrates the skin. The portion of the light penetrating the skin should be determined for each wavelength. A spectrograph, therefore, would seem to be the ideal instrument for such an investigation. However, the scattered radiation which penetrates the skin could not be measured with a spectrograph unless the skin was suspended immediately in front of the plate. Large homogeneous pieces of skin then would be required and it would be difficult to obtain such large pieces of skin which would have the same thickness all over. By using a cassette with a small hole over which the skin can be suspended and suitable light filters, it is possible to find out how much light of certain parts of the spectrum penetrates the skin altogether. We adopted both of these methods of investigation and shall describe the arrangements and results below.

For the first part of the investigation we used an ADAM HILGER spectrograph no. C and a sector photometer. A piece of skin was stretched over a hole in a rubber stopper and this stopper was attached to an absorption chamber from which the quartz windows had been removed. The chamber was mounted in the sector photometer so that a comparison spectrum could be exposed on the plate next to the absorption spectrum. (Special measurements were made

to determine how much light the rubber stopper cut off.) The sectors could not be kept rotating throughout the exposures due to the great difference in time of exposure between the two spectra. Fluctuations in the intensity of the light source, therefore, would be one source of error. The approximation that the blackening is determined by the light intensity multiplied by the time of exposure was used for the calculation of the transparency. This brings in another error on account of the great difference in the time of exposures. Due to the variation in the thickness and absorption of different samples of skin the errors mentioned are relatively negligible.

The pathologist at the Institute, Dr A. THIBAUDEAU, supplied us with several samples of human skin. This skin was about $2^1/_2$ mm thick including the adhering fat and varied slightly in color from white to a light tan. The exposure required to produce a suitable blackness on the plate through this skin was, however, too long to be practical. The biologist at the Institute, Mr M. MARSH, then proposed that we use the skin of mice four to six days old, which is about $^1/_2$ mm thick and free from hair. He also supplied us with the required animals, the skins of which were used immediately after killing and skinning the mice. An exposure of eight hours with an under water spark between tungsten electrodes as a light source gave a blackening on the plate that could be traced down to 315 $\mu\mu$. A comparison spectrum which was produced in one minute showed the same intensity as the absorption spectrum at 450 $\mu\mu$ and could be traced beyond 230 $\mu\mu$. This result shows that only a very small fraction of the ultraviolet light goes straight through $^1/_2$ mm of skin. A 400 watt Mazda lamp taken from a stereopticon was used as a light source for further study of the absorption in the visible region as it gave a good continuous spectrum there of much greater intensity than the under water spark. It faded out at 315 $\mu\mu$. The absorption curve in fig. 1 was obtained with help of this light source. A little more than 0.1 % of the red light passes straight through $^1/_2$ mm of mouse skin. The shorter the wavelength the less the percentage of light passing through. About one half as much of the blue passes through as of the red. At 450 $\mu\mu$ the curve starts to slope down sharply and already at 415 $\mu\mu$ the penetrating part has fallen down to about 0.01 %. At this point is another increase in the absorption which probably is due to the presence of hemoglobin. Due to the great absorption in ultraviolet quantitative measurements were not made for shorter wavelengths than 415 $\mu\mu$ but it could be seen on the first plate that a real absorption band existed between 420 and 390 $\mu\mu$. Below 390 $\mu\mu$ the intensity on the plate decreased slowly with the wavelength until about 340 $\mu\mu$

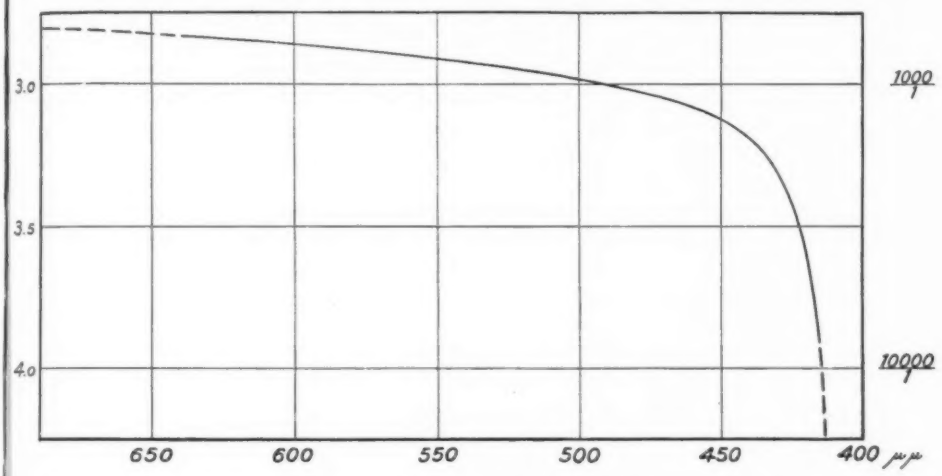

Fig. 1. Curve showing proportion of incident light which goes straight through 1/2 mm thick mouse skin. Abscissae = wavelength in $\mu\mu$. Ordinate (left) the logarithm of the relation between the intensity of the incident light and the intensity of the light passing straight through the skin. To the right is shown where this relation is 1,000 to 1 and 10,000 to 1.

where it again started to decrease faster, fading out completely between 315 and 310 $\mu\mu$.

The percentage of radiation of any wavelength which penetrates the skin, e. g. during a sun bath is of course greater than the amount shown in curve I by the amount which is scattered through the skin. It could be measured directly if the photographic plate were placed close behind the sample of skin. The reasons why such measurements cannot very well be made with a large spectrograph have already been given. The penetration of certain regions of the light was, therefore, determined in the following way. Two round holes 3 mm in diameter were cut in the bottom of a cassette and covered with an automatic shutter. The cassette was loaded with a panchromatic plate with the sensitive film towards the holes and was placed at a distance of 3.55 m from the positive crater of a carbon arc lamp. When the arc was burning steadily with a load of 10 amperes the part of the plate behind the holes was exposed for a short time. This procedure was repeated with variation of the time of exposure until it was found that an exposure of one second gave a suitable blackness. An Eastman gelatin filter which lets through light between 510 and 700 $\mu\mu$ was then placed immediately in front of the plate (at 1 cm distance) and similar exposures

were made until the time was determined which gave the same blackness as an exposure of one second produced without any filter. The blackness was measured with a Martens polarization photometer. The corresponding time was further determined for the following filters: Eastman no. 58B2, Eastman 49C4 and Corning glass 586A.W., which let through light between 480 and 620 $\mu\mu$, 360 and 500 $\mu\mu$ and 350 and 382 $\mu\mu$ respectively.

The next step was to cover up one of the holes with mouse skin about $^1/_2$ mm thick (placed at 4 mm distance from the plate) and determine the relation between the time necessary to produce the same blackness on the spot of the plate which was covered by the skin and on the spot which was uncovered. This was done both without any filter and with each one of the four filters. Finally this whole procedure was repeated with about $2^1/_2$ mm thick human skin instead of the mouse skin. The results of these experiments are shown in table I.

Table I

Filter	Light transmitted	Time of exposure in seconds		
		no skin	$^1/_2$ mm thick mouse skin	$2^1/_2$ mm thick human skin
0	—	1	3	30
1 E.15G	510—700	15	20	90
2 E.58B2	480—620	10	240	1,800
3 E.49C4	360—500	10	360	2,700
4 C.586A.W.	350—382	30	3,600	very long

Tables II and III have been calculated from the data in table I. The percentage of light transmitted through mouse skin and human skin has been calculated by dividing the time necessary to give the standard blackness on the plate without any skin (column 3 in table I) by the time it took to produce the same blackness with mouse and human skin respectively, and multiplying by 100. Columns 4 and 5 in table I give the time it took in seconds to produce the standard blackness through mouse skin and human skin respectively, and column 6 in table II shows how much longer time it takes to produce this blackness through human skin than through mouse skin. The differences between the figures in this last column are small considering the fluctuations of the intensity of the light source and the difference between different samples of skin. Table III gives the relative transparency of mouse skin and human skin for the light which

Table II

Filter	Percent of light transmitted		column 4 / column 3	column 5 / column 3	column 5 / column 4
	mouse skin	human skin			
0	33	3.3	3	30	10
1	75	16.7	1.3	6	4.5
2	4.2	0.6	24	180	7.5
3	2.8	0.4	36	270	7.5
4	0.8	?	120	very large	?

Table III

Filter	Light transmitted	Relative transparency		
		mouse skin	human skin	human skin / mouse skin
0	—	1	1	1
1	510—700	$2^1/_2$	5	2
2	480—620	$^1/_8$	$^1/_6$	$1^1/_3$
3	360—500	$^1/_{12}$	$^1/_9$	$1^1/_3$
4	350—382	$^1/_{40}$	?	?

passes through the different filters in relation to the unfiltered light. This was obtained from table II.

Discussion of Results

The values of light transmission obtained by means of the filters are not very accurate. Such filters do not completely prevent light of other wavelengths than the ones tabulated to reach the skin and the plate. Another error is due to the distance between the skin and the plate. This distance was 4 mm while the diameter of the hole was only 3 mm. Therefore, some of the light scattered through the skin was lost. A third error was introduced by the fluctuations of the intensity of the light from the arc. Due to the small pieces of skin needed, good samples could be selected, but it is evident that they must have varied somewhat in thickness.

By comparing values which can be obtained from curve I with the figures in column 2 of table II it will be noticed that the amount scattered through the $^1/_2$ mm thick skin of young mice is about 100 times as great as the amount going straight through it.

From tables II and III it can be infered that the relation of the total amount of light penetrating 1/2 mm thick mouse skin and 2 1/2 mm thick human skin is about 10 to 1. It is evident that for the more penetrating rays towards the red end of the spectrum the relation is smaller than 10 to 1 and that it is greater than 10 to 1 for the less penetrating ultraviolet rays. The curve for 2 1/2 mm thick human skin which would correspond to curve I for mouse skin evidently has the same general shape. It ought to start around 3.5 at 650 $\mu\mu$ and have a somewhat greater slope than the curve in fig. 1. The reasons we did not determine the human skin curve experimentally were that so long exposures were required that it seemed almost impossible to keep the skin in good condition throughout the exposures and that the plate may during this time receive an appreciable amount of stray radiation.

We have not been able to find in the literature any investigations quite comparable with the ones just described. HANS JANSEN made some qualitative determinations of the penetrability of ultraviolet rays as early as 1903 (1). SCHMIDT measured the absorption of light rays by skin and by some other tissues of animals in 1908 (2). He found that 3 mm thick skin let through 0.4 % of the rays for $\lambda = 470$ $\mu\mu$, 6.2 % for $\lambda = 550$ $\mu\mu$, 25.5 % for $\lambda = 750$ $\mu\mu$, 26.5 % for $\lambda = 800$ $\mu\mu$ and 12.1 % for $\lambda = 1{,}000$ $\mu\mu$. K. A. HASSELBALCH determined the percentage of violet and ultraviolet radiation penetrating different thicknesses of human skin (3) and found that a 0.5 mm thick layer of skin let through 7 % for $\lambda = 436$ $\mu\mu$, 5 % for $\lambda = 405$ $\mu\mu$, 3.0 % for $\lambda = 366$ $\mu\mu$, 1.3 % for $\lambda = 334$ $\mu\mu$ and 0.3 % for $\lambda = 313$ $\mu\mu$. The values obtained in the second part of our investigation agree qualitatively with the values cited here. They are numerically lower as would be expected for the reason that we measured only the amount of radiation scattered forward within 40°.

SUMMARY

1. The percentage of light rays striking the skin taken from young mice at normal incidence which goes straight through has been measured for wavelengths between 700 and 415 $\mu\mu$ and traced down to 315 $\mu\mu$ by means of a quartz spectrograph and a sector photometer. The results are registered graphically in fig. 1 and are discussed in the text.

2. The percentage of light rays striking the skin taken from young mice (1/2 mm thick) and from human bodies (2 1/2 mm thick) respectively at normal incidence which goes straight through and is scattered through within an angle of 40° has been measured for certain spectral regions by means of light filters and photographic plates. The total amount thus penetrating the skin has been found to be about 100 times greater than the amount which goes straight through the skin.

3. The first part of the investigation was made with the object of determining the relation between wavelength and penetrability. We have not found in the literature any parallel experiments recorded. The second part was undertaken in order to determine the approximate value for the amount of radiation penetrating the skin during radiation of the body. It has been compared with some earlier work which partly covered the same wavelength regions and a qualitative agreement was found.

ZUSAMMENFASSUNG

1. Von Lichtstrahlen, welche unter normalem Einfallswinkel ein Stück jungen Mäusen entnommener Haut treffen, wurde der prozentuelle Anteil, der gerade durchgeht, mittels eines Quarzspektrographen und eines Sektorphotometers für Wellenlängen zwischen 700 und 415 $\mu\mu$ gemessen, und Durchgang von Licht der Wellenlängen bis zu 315 $\mu\mu$ hinab noch konstatiert. Die Resultate sind in Fig. 1 graphisch registriert und im Text erörtert.

2. Von Lichtstrahlen, die in normalem Einfallswinkel auf ($^1/_2$ mm dicke) jungen Mäusen entnommene Haut resp. ($2^1/_2$ mm dicke) Haut von Menschen auffallen, wurde der Prozentanteil, der die Haut gerade passiert und derjenige der sie in einem Winkel von 40° zerstreut passiert, für gewisse spektrale Regionen mit Hilfe von Lichtfiltern und photographischen Platten gemessen. Es zeigte sich, dass die Gesamtmenge der zerstreuten Strahlen, welche die Haut so durchdringt, ungefähr 100 mal grösser ist als die Menge, welche die Haut geradlinig passiert.

3. Der erste Teil der Untersuchung beabsichtigte die Beziehung zwischen Wellenlänge und Penetrabilität zu bestimmen. In der Literatur haben wir keine parallelen Versuche erwähnt gefunden. Der zweite Teil der Arbeit hatte als Ziel den annähernden Wert der Strahlungsmenge zu bestimmen, welche die Haut bei Bestrahlung des Körpers durchdringt. Die Resultate wurden mit denen einiger früherer Arbeiten verglichen, welche zum Teil dieselben Wellenlängenregionen betrafen, wobei sich eine qualitative Übereinstimmung ergab.

RÉSUMÉ

1. Le pourcentage de lumière qui, frappant à une incidence normale la peau de jeunes souris, traverse complètement cette peau, a été mesurée pour des longueurs d'onde de 700 à 415 $\mu\mu$ et notée jusqu'à 315 $\mu\mu$, à l'aide d'un spectographe à quartz et d'un photomètre à secteurs. Les résultats sont reproduits graphiquement à la fig. 1 et discutés dans le texte.

2. Le pourcentage de lumière qui, frappant la peau de jeunes souris ($^1/_2$ mm d'épaisseur) ou la peau humaine (2.5 mm d'épaisseur), traverse entièrement à une incidence normale ou diffuse à travers la peau pour des incidences atteignant 40°, a été mesuré à l'aide d'un photofiltre et de plaques photographiques pour diverses régions du spectre. On a établi que la quantité totale de lumière ainsi absorbée par la peau est environ 100 fois plus grande que la quantité traversant entièrement la peau.

3. La première partie des présentes recherches a été effectuée dans le but d'établir le rapport existant entre la longueur d'onde et la pénétrabilité. Nous

n'avons trouvé nulle part, dans la littérature, de parallèle de cet ordre. La seconde partie de ce travail a eu pour but de déterminer la valeur approximative de la quantité de lumière traversant la peau au cours d'irradiations du corps. Ces résultats ont été comparés à des travaux antérieurs concernant des régions de même longueur d'onde, et cette comparaison a permis de constater avec ces travaux une concordance qualitative.

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ZUR VERSTÄRKUNG DER RÖNTGENWIRKUNG MITTELST INTRAVENÖSER DEXTROSEINJEKTION NACH E. G. MAYER M. D.[1]

von

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Ernst G. Mayer hat in meinem Institut im Allgemeinen Krankenhaus in Wien und an der laryngologischen Klinik Professor Hajek's gefunden, *dass die Röntgenbestrahlung von benignen und malignen Tumoren viel wirksamer ist, wenn vor und nach derselben intravenös Dextrose (Traubenzucker, Osmon 33 %) injiziert wird.* Er hat in der Gesellschaft der Ärzte in Wien am 29. Januar 1926 eine Mitteilung darüber gemacht, einige überraschende Fälle gezeigt und über 20 andere berichtet. Mehr als die Hälfte hat die verbessernde Wirkung erkennen lassen. In der Diskussion hat Professor Hajek auseinandergesetzt, dass die Effekte wirklich sehr bemerkenswert sind und alles, was man in dieser Richtung bisher gesehen hat, bedeutend übertrifft.

Die Röntgenbestrahlungen wurden dabei anfangs nach der in meinem Institut üblichen Methode mit fast vollen H. E.-Dosen pro Feld und 1—2 Tagen Pause zwischen den Feldern vorgenommen, später mit $^3/_4$ HED.

Zur Bewertung der Mitteilung Mayer's über seine *Verbesserung des primären Bestrahlungseffektes bei Tumoren durch intravenöse Dextroseverabreichung* muss man den Verlauf *seiner* Fälle mit dem Verlauf von Fällen vergleichen, bei welchen ausschliesslich Bestrahlung angewendet wurde.

Was die Röntgenstrahlen allein in der Therapie der malignen und benignen Tumoren bisher geleistet haben, ist leicht zu sagen: Bei den *Sarkomen* jeder Art, inclusive die Lymphosarkome, haben sie in ca. 30 % der Fälle den *primären Schwund* der Tumoren bewirkt und die Verlängerung des Lebens dieser Fälle.[2] Die Verkleinerung begann bei Sarkomen nach einigen Tagen und dauerte einige Wochen, also *kurze Latenzzeit* und *rasche Verlaufsgeschwindigkeit.* Bei *Karzino-*

[1] Nach einer Diskussionsbemerkung zum Vortrag von Mayer in der Ges. d. Ä. in Wien.

[2] Jüngling's Statistik.

men war die Wirkung viel schlechter und auch viel langsamer. In nur etwa 2 % der gesamten Fälle aller Localisationen fünfjährige Heilungen alles in allem gerechnet. Bei den günstigen Portiokarzinomen des Uterus 10—20 %, dafür bei vielen anderen Lokalisationen null % Erfolg. Die *primäre Verkleinerung* der günstigen Karzinomfälle begann 2—6 Wochen nach der Bestrahlung und gedieh im Laufe von Monaten in verschiedenem Masse, also *lange Latenzzeit* und *langsame Rückbildungsgeschwindigkeit*.

Die von MAYER mit Bestrahlung und Osmon behandelten Karzinomfälle, vorwiegend solche, welche aus dem rhinolaryngologischen Bereiche stammen, die ich z. T. mitbeobachtet habe, weichen von dem bisher Bekannten in zweifacher Hinsicht ab. Erstens in der Latenzzeit und zweitens in der Rückbildungsgeschwindigkeit. Die primäre Verkleinerung tritt in viel kürzerer Zeit ein, fast in soviel Tagen als früher Wochen vergingen; also *kurze Latenzzeit* und *rasche Rückbildung*. Zweitens traten diese Wirkungen bei Fällen auf, welche sonst erfahrungsgemäss für blosse Röntgenbehandlung ungünstig sind, auch solchen, in welchen vorher alleinige Röntgenbestrahlung schon vergebens angewendet worden ist. Wenn man sich des bisherigen Verlaufes röntgenbestrahlter Sarkome erinnert, könnte man sagen: Die Karzinome nehmen unter Dextrosewirkung den röntgentherapeutischen Charakter der Sarkome an.

Angesichts dieses Ergebnisses einer Kombinationsbehandlung interessiert es vielleicht, zu hören, welches die *bisherigen Ergebnisse* der bekannten und einiger von uns unternommenen *Kombinationsversuche* waren. Diese Versuche haben drei Wege eingeschlagen, um den Effekt der Röntgenstrahlen, welche bisher ausser der Exstirpation der operablen Tumoren das einzige Mittel mit markanter Wirkung waren, zu verbessern. Man konnte erstens solche Mittel, welche für sich allein eine deutliche, aber unzureichende Wirkung üben, mit Röntgenbestrahlung kombinieren und dabei einen in der Hauptsache *additiven Effekt* von verschiedener Grösse erwarten. Man konnte zweitens *vor* der Röntgenbestrahlung oder gleichzeitig mit ihr Mittel anwenden, auf Grund der Annahme, dass sie die nachfolgende Röntgenwirkung steigern, also einen *sensibilisierenden Effekt* hervorrufen. Endlich konnte man *nach* der Bestrahlung Mittel versuchen, in der Annahme, dass sie die ablaufende Röntgenwirkung erhöhen, also einen *adjuvierenden* Effekt haben.

Angesichts der berechtigten Hoffnungen, welche die Röntgenbestrahlung von Tumoren erregt hatte — in den wenigen günstigen Fällen war ja das Schwinden der Tumoren überaus ermutigend — aber angesichts des verzweifelt geringen durchschnittlichen Erfolges, wurde in der letzten Zeit nichts Denkbares unversucht gelassen. In

der Gruppe der *additiven* Kombinationsversuche nenne ich die BIER'sche Umspritzung der Tumoren mit *Eigenblutserum* und die zahlreichen Tumor-Sera, von welchen man, wenn sie für sich allein angewendet wurden, Günstiges berichtete. Ferner als neu — ich hatte bisher keine Gelegenheit, davon zu sprechen — für oberflächliche und ulzerierte, also der osmotischen Durchdringung in gewissem Masse zugängliche Tumoren, besonders für präkanzeröse Ulzerationen, einen zweifellosen Effekt von Scharlachrot und von Granugen. Bei oberflächlichen, ulzerierten oder künstlich exfoliierten Karzinomen hat ferner nach ANDERSEN in Kiel *Kochsalz*, in hoher Konzentration als Brei mit Wasser angerührt und für 24 bis 48 Stunden aufgelegt, einen ziemlich tiefgreifenden raschen Effekt, von dem allein ich schon Epitheliomheilungen gesehen habe. Für oberflächliche und tiefliegende oder tiefgreifende Karzinome wurden die *Tumorautolysate* von JOVANOVIC (Belgrad) und das von BAUER (Wien), ferner ein *Tumorcidin*, dann das neue *Tumorserum* von BLUMENTHAL angewendet und in Kombination gezogen. Allein die Kombination dieser Mittel mit Röntgenstrahlen bringt anscheinend nicht mehr hervor als die reine additive, übrigens bescheidene Wirkung und die ersteren zeigen in der Tiefe jedenfalls nur eine reine Röntgenwirkung. Man kann sie ebenso gut jede für sich also nacheinander anwenden. Im Sinne der *sensibilisierenden* oder der *adjuvierenden* Wirkung wurden die an sich unwirksamen *parenteralen* Applikationen von *Kochsalz* und von *Eiweiss*, ferner Metallcolloide und die *Fiebertherapie* versucht. Im Gegensatz zu manchen Mitteilungen haben wir auch bei ihnen keinen Anlass Gutes zu erwarten.[1]

Die *Dextrose*, die ERNST GEORG MAYER versucht hat, lag einerseits seit WARBURG's Angabe über den vorwiegenden Gärungsstoffwechsel der Mäusekarzinome sehr nahe. Anderseits lag sie wieder ferne, weil sie ja nach WARBURG gerade das Nährmittel der Karzinome wäre, also eher ihr Entzug eine Aussicht bot. Auf diesem Wege hatte ja auch SILBERSTEIN mit *Insulin* einige Erfolge zu verzeichnen. Wer also an Dextrose dachte, musste bei der nächsten Überlegung wieder von ihr Abstand nehmen. Das ist wohl der Grund, warum sie bisher nicht versucht wurde. Erst über den von ERNST MAYER eingeschlagenen Gedankengang konnte es zu einem Versuch kommen.

Im Ganzen liegen natürlich nur *Anfangserfolge*, nicht Heilungen vor, welche aber einerseits viel mehr versprechen, als die Röntgenstrahlen bisher geleistet haben, anderseits schon in einer *Reihe wahrhaft jammervoller Fälle grossen Nutzen gebracht* haben.

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[1] Seit dieser Besprechung (Juli 26) sind die aus der Klinik Opitz mitgeteilten Versuche hinzugekommen.

ZUSAMMENFASSUNG

Übersicht über die Effekte der Sensibilisierung von Karzinomen durch vorausgehende intravenöse Dextrose-Injektion nach E. G. MAYER, Wien, auf Grund der Mitbeobachtung und eigener Beobachtungen: Eine viel grössere Zahl von Karzinomen sprechen auf Bestrahlung an, günstige Wirkung tritt rasch ein und erreicht schnell ihr Maximum. Die übrigen bisher versuchten additiven, sensibilisierenden und adjuvierenden Mittel haben keine nennenswerten Effekte gebracht.

SUMMARY

A review, on the basis of observations by the author and others, of the effects of preliminary intra-venous injection of dextrose — according to the method of E. G. MAYER, Vienna — on the sensibility of carcinomata to röntgen treatment: a much greater number of cases are benefited by the rays, a favourable effect rapidly ensues and a maximum result is quickly obtained. Other adjunct means that have so far been tried in order to increase the sensibility to treatment, have had no effect worth mentioning.

RÉSUMÉ

L'auteur résume les effets de la sensibilisation des carcinomes par l'injection intra-veineuse préalable de dextrose, d'après la méthode de E. G. MAYER, de Vienne, en s'appuyant sur l'observation de celui-ci et sur des observations personnelles. Une grande majorité de carcinomes est justiciable de l'irradiation; celle-ci détermine un effet favorable rapide qui atteint bientôt son maximum. Les autres agents additionnels, sensibilisateurs et adjuvants précédemment essayés n'ont donné aucun résultat appréciable.

FROM THE ROENTGEN DEPARTMENT AT SAHLGREN'S HOSPITAL, GOTHENBURG
DIRECTOR: DR. FR. VON BERGEN

A DEVICE FOR THE EXACT PLACING AND FIXATION OF THE HEAD IN SKIAGRAPHY, WITH PARTICULAR REFERENCE TO THE EXAMINATION OF THE ACCESSORY NASAL CAVITIES

by

Henning Odqvist

In roentgen examination of the accessory nasal cavities it is, as is well known, of the greatest importance to be able to accurately place the head in its sagittal axis, to obtain fully comparable pictures of the right and the left side. In particular is this important in the examination of the ethmoid cells and the maxillary antri. To do this manually and obtain full exactitude without any special appliance is almost impossible.

To obtain an accurate position of the head in sagittal direction I have for some years made use of an arrangement that will be described more in detail below. The underlying principle is as follows:

Presuming that the external auditory meatus on both sides are, as a rule, symmetrically placed, I have devised an apparatus to enable these to be placed in the same horizontal plane. Consequently, the head will then come to be accurately postured in the sagital plane. The apparatus may be thus described: To each end of an about 5 cm. long, somewhat curved, horizontal metallic plate there is attached and jointed a metallic stem. These stems are of similar appearance as the tubes of a binaural stethoscope and supplied with small bone buttons to be put into the ears in a manner to be further described. To the centre of the horizontal pièce of metal a rod is vertically attached on which a shell is sliding. This shell is jointed with the "ear-tubes" by means of two pieces of metal which themselves are connected with the horizontal piece by two short spiral springs. On the "ear-tubes" being moved away from the middle line the angulation will consequently be equal on

both sides. With the two free ends of the stems placed on a water level, two circle-graded scales are soldered at right angles to each other at the centre of the horizontal piece right above the previously mentioned metallic rod, and from the centre of these scales a pendulum is suspended which at the fixation of the scales should be opposite the figure O. (Figs. 1 and 4.)

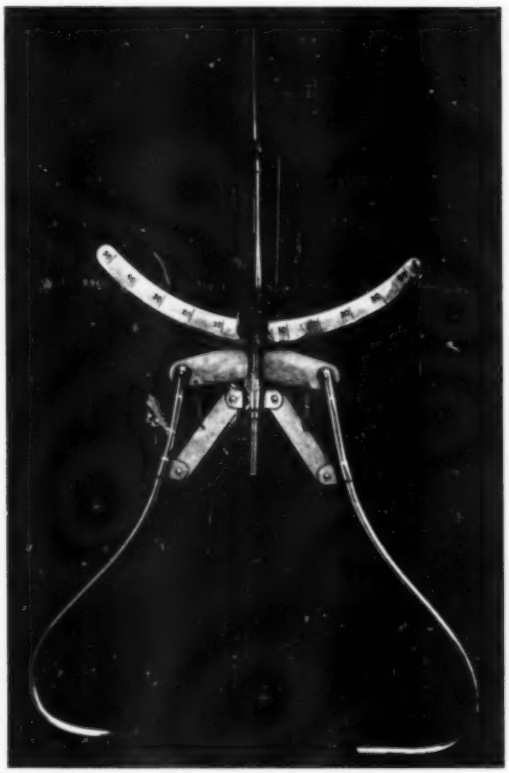

Fig. 1.

For fixation of the head in this position, I have devised the following apparatus.

To a strong ebonite plate, permitting the taking of 18×24 films, wide side frames are attached. In the forepart of these there are two transverse grooves in which two strong lateral supports can be slid to and fro; they can be secured in any position by means of screws. Along the inner side of each support a leather strap is tightly suspended between two small wooden blocks; to one of the frames a water-level is attached. At the fore and aft-part of the right frame there are two screws by which this part of the apparatus can be raised and lowered and carefully adjusted to the water-level. (Fig. 2.)

The posturing and fixation of the patient is done thus: He takes a prone position with his face against the film on the ebonite plate. To avoid shifting the head for the different positions in roentgen-raying the frontal and maxillary cavities, a thin aluminium plate may be inserted above the film against which patient supports his nose and forehead.

Should the examination table be one with padded top, a firm

wooden board may be inserted with advantage underneath the fixation apparatus so as to enable the regulating screws by which this is adjusted to the water-level, to serve their purpose in a more satisfactory manner. The side supports are pushed up to the sides of the scull immediately above the ears, the straps thereby adapting themselves to the shape of the head. The supports are provisionally fixed. The ear pieces of the levelling apparatus are then put into the auditory canals, the buttons being directed obliquely forwards. These are pressed carefully upwards against the bony wall of the canal and the head is rotated until the pendulum is opposite "O"

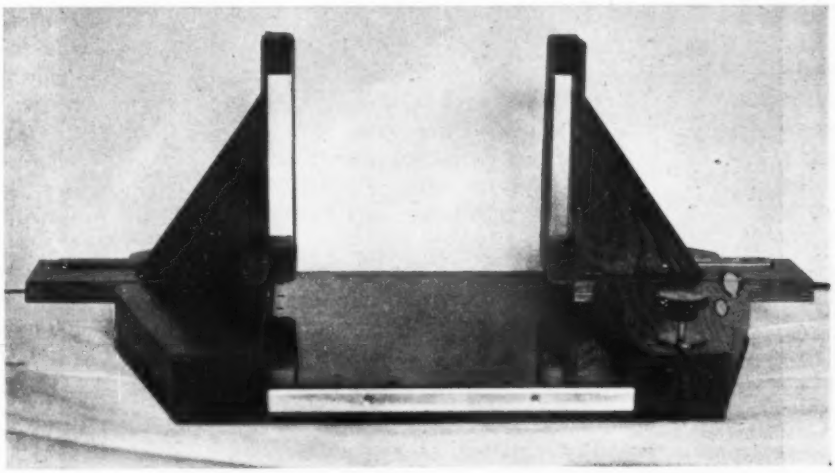

Fig. 2.

on the frontal scale. The lateral supports are now firmly fixed and the levelling apparatus removed. The diaphragm is carefully adjusted by water-level in the usual way and the centred roentgen tube is applied. (Figs. 3 and 4.)

For those who in examination of the sinuses are in the habit of putting the film at a certain angle with the under-structure, a wedge can with advantage be inserted underneath the apparatus.

After some experience the manipulation and fixation of these appliances take less than a minute.

On skiagraphy of the maxillary antri it is also important to note the position of the neck in relation to the head. One should therefore be careful in arranging the shoulders symmetrically.

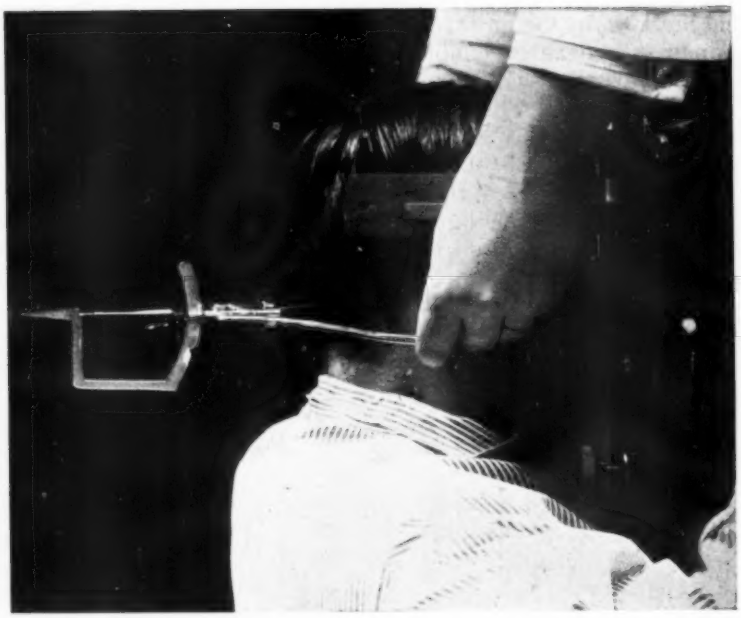

Fig. 4.

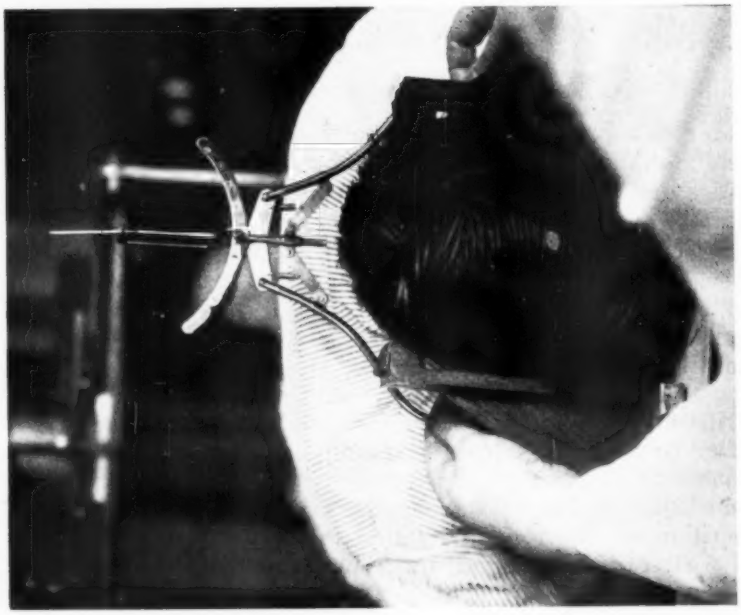

Fig. 3.

Not only in the examination of sinuses, however, does this arrangement prove its usefulness, but also in cases where it is wished to take identical pictures in an oblique direction, e. g. from the right and the left side of the head.

Of fixation apparatus for the head in the examination of the accessory cavities there are some of older date described in the literature (RIEDER, SCHWERDTFEGER, ROTAX, SCHMIDT and others). These are made for use in sitting position, but are probably no longer used, at least not in Sweden.

Since my apparatus was constructed an arrangement for fixing the head has been published in America by Dr. GRANGER, 1923. He makes use of an apparatus where a plate is excavated to receive the nose. The plate is placed above the film. At the sides of the apparatus there are two adjustable supports which are pressed against the sides of the heads. This arrangement alone would scarcely seem to allow any fully exact posture of the head. An excellent, but more complicated apparatus for placing and adjusting the head at different angles has recently been published in Acta Radiologica by Dr. LYSHOLM. The above described apparatus, devised by me, is, as already stated, especially designed for roentgen examination of the accessory nasal cavities and lends itself well for use in daily practice. As the roentgen pictures obtained by it have gained considerably in definition I have thought it worthy of publication.

The technical details of these apparatus have been elaborated by Mr. B. SELDÉN, engineer in A. B. Elema, Gothenburg.

SUMMARY

The author describes a device for placing and fixing the head with particular reference to the roentgenological examination of the accessory nasal cavities. The apparatus can also be used for obtaining identical, oblique, lateral positions of the cranium. The device, based on the assumption of the external auditory meatus being symmetrically situated, enables these to be placed in the same horizontal plane, whereby the cranium comes to obtain an exact position in its sagittal axis. From this initial position the cranium may then be turned to the right or the left side along a circular scale. The fixation arrangement is made up in the shape of adjustable, strop-like, side-supports which adapt themselves according to the shape of the cranium.

ZUSAMMENFASSUNG

Verfasser beschreibt eine Fixations- und Einstellungsvorrichtung für den Kopf, speziell mit Rücksicht auf die Röntgenuntersuchung der Nebenhöhlen der Nase. Die Apparate sind auch für identische, schräge Seiteneinstellungen des Schädels zu verwenden. Die Einstellungsvorrichtung geht von der Annahme aus, dass die Meatus acust. ext. auf beiden Seiten symmetrisch

angelegt sind. Der Apparat stellt beide in dieselbe Horizontalebene ein, und man erhält dadurch eine exakte Einstellung des Schädels in der sagittalen Achse. Von dieser Ausgangsstellung kann das Kranium dann nach einer Kreisskala rechts oder links gedreht werden. Die Fixationsvorrichtung besteht aus verschiebbaren, streichriemenartigen Seitenstützen, die sich nach den Seiten des Kopfes formen.

RÉSUMÉ

L'auteur décrit un dispositif permettant de réaliser la mise au point et la fixation de la tête et plus particulièrement destiné à l'examen des cavités annexes des fosses nasales. Ce dispositif est également utilisable pour la mise au point identique et oblique du crâne. L'appareil repose sur l'hypothèse de la symétrie des deux conduits auditifs externes de chaque côté de la ligne médiane; il réalise la mise au point de ces deux conduits auditifs dans un même plan horizontal et détermine ainsi une mise au point sagittale rigoureuse du crâne. Partant de cette position initiale, on peut effectuer alors une rotation du crâne à droite ou à gauche, en suivant une échelle circulaire. L'appareil de fixation a la forme d'un appui latéral ajustable se modelant sur les faces latérales du crâne.

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AUS DER RÖNTGENABTEILUNG DES KRANKENHAUSES SABBATSBERG
CHEFARZT: DR. M. SIMON

EINE BLENDENVORRICHTUNG VOM IRISTYP FÜR DEN GEBRAUCH IN DER RÖNTGENDIAGNOSTIK[1]

von

Arvid Lundqvist

Um qualitativ gute Röntgenbilder zu erreichen, ist ausser scharfzeichnenden Röntgenröhren eine gute Abblendungstechnik erforderlich, worauf nahezu von Beginn der Röntgenaera an von mehreren Seiten aufmerksam gemacht wurde.

Die gebräuchlichen Blendentypen sind teils Zylindermodelle — an amerikanischen Apparaten zu einer konischen Form modifiziert — teils lose, einschiebbare Lochblenden an Zylindern oder ohne solche. Bei Veränderung der Blendengrösse sind die verschiedenen Zylinder oder Lochblenden umzutauschen, was zwischen den verschiedenen Expositionen häufig sowohl zeitraubend als lästig sein kann. Vor einigen Jahren war eine regulierbare Lochblende vom Iristypus ohne Zylinderansatz im Handel erhältlich, die jedoch aus verschiedenen Gründen keine grössere Verbreitung gewann und durch die obenerwähnten Modelle völlig verdrängt wurde. Ohne etwas von dem Vorhandensein dieser verstellbaren Irisblende zu wissen, habe ich eine Blende vom Iristyp mit Lamellen vom halben Blendendurchmesser verfertigen lassen, die am unteren Ende eines Zylinders sitzt, und habe sie nahezu 1 Jahr bei der täglichen Arbeit in der Röntgenabteilung des Krankenhauses Sabbatsberg in Gebrauch gehabt, während welcher Zeit sie die Arbeit in bedeutendem Masse erleichterte, so dass eine Mitteilung darüber gerechtfertigt sein dürfte. Die Konstruktion geht aus den beigefügten Abbildungen hervor. Die Lamellen sind aus 3 mm dickem Kupferblech verfertigt, jede von

[1] Nach einem Vortrag, gehalten im Schwedischen Verein für medizinische Radiologie am 30. Mai 1926.

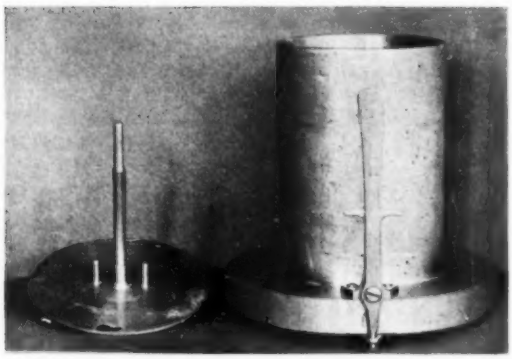

Fig. 1.

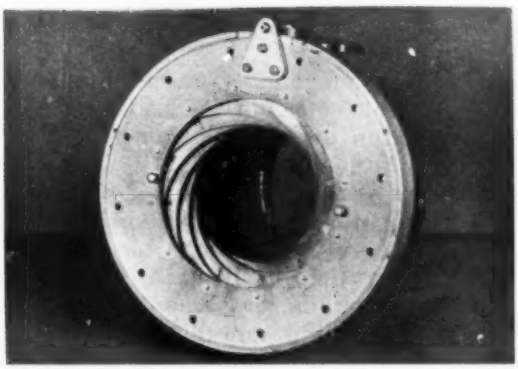

Fig. 2.

ca. 3 cm Breite und verstellbar, so dass die Öffnung mittelst eines an der Aussenseite sitzenden Hebels von 4 bis ca. 14 cm variiert werden kann.

Der Zylinder wird am gewöhnlichen Kompressionszylinder von Albers-Schönberg befestigt, kann aber ebensogut auf einer besonderen Fussplatte sowohl am Trochoskop, als am Durchleuchtungsrahmen von Forssells Modell, sowie an den Röhrenhaltern der amerikanischen Stative angebracht werden. Mit Hilfe einer einfachen graphischen Aufstellung kann die Blendenöffnung für jeden Fokus-Plattenabstand von 5 cm Bilddiameter und 40 cm Abstand z. B. bis 30 cm Bilddiameter und 70 cm Abstand in entsprechender Grösse bestimmt werden. Die Länge der zur Blende gehörenden

Tube beträgt 13 cm, was bei der Verwendung am Trochoskop und am Durchleuchtungsstativ einen bedeutenden Vorteil hat, indem es ausserdem eine Extra-Abblendung mit Zylindereffekt vor der gewöhnlichen einstellbaren Blende ermöglicht, wodurch die Schärfe des Radiogrammes gesteigert wird, und man deutlichere Bilder erhält. Die Einstellung der Blendenöffnung geschieht dabei mittelst Fernregulierung in der gewöhnlichen Weise.

An Stelle der konischen Zylinderblenden vom amerikanischen Modell an Universaltischen mit eingebauter Sekundärblende ist die Verwendung des angegebenen Iristyps gleichfalls zu empfehlen, in diesem Fall aber mit etwas grösserer Dimension, wobei man auf 75 cm Abstand mit einer Tubuslänge von 13 cm einen Bilddiameter von 10 cm bis zu 42 cm erhalten kann. Der Vorteil hierbei ist, dass man zwischen gewöhnlichen Skelettaufnahmen mit kleinem Plattenformat und Aufnahmen von Übersichtsbildern mit grossem Plattenformat bei Verwendung der Sekundärblende die Blende nicht umzutauschen braucht. Auch verringert sich die bei dieser Apparatur — besonders bei Verwendung von stärkeren Spannungen — vorhandene Tendenz zu grauen flauen Bildern.

Bei Spezialaufnahmen über einzelne Wirbel unter Verwendung der Åkerlundschen Sekundärblende erhielt man bei Kombination mit Kompression und der geschilderten einstellbaren Irisblende ausserordentlich schöne Radiogramme; wesentlich schärfer und deutlicher als die Bilder, die man ohne Kompression und Abblendung erzielt.

Für Röntgenröhren vom neuen Röhrentypus — Metallixröhren — dürfte die Irisblende in einer kleineren Ausführung gleichfalls leichthantierlich sein.

Bei Skelettaufnahmen wird am besten unmittelbar unter der Blende ein abnehmbarer Richtstab angebracht, wobei die Röntgenröhre zwischen den verschiedenen Einstellungen nicht fortgenommen zu werden braucht.

Bei gegen die Platte senkrecht verlaufender Strahlenrichtung erhält man einen scharfen, nahezu runden Rand mit vollständiger Abblendung der Umgebung; bei im Winkel gegen die Platte verlaufender Strahlenrichtung erhält man einen etwas zackig unregelmässigen Rand, dadurch dass immer eine Lamelle auf der anderen liegt. Die Abblendung gegen die Umgebung ist auch hier vollständig scharf.

Wie oben angedeutet wurde, trägt die Blende zur Erzielung von guten Radiogrammen dadurch bei, dass sie eine gute Abblendung ermöglicht und bei der Röntgenarbeit sowohl Mühe als Zeit erspart.

Die Blende ist bei Jährns Elektriska Aktiebolag, Stockholm, erhältlich.

ZUSAMMENFASSUNG

Verf. empfiehlt die Verwendung einer Blende von Iristyp — in Kombination mit einem Zylinder — an Stelle der gebräuchlichen Zylinder- und Lochblenden in der Röntgendiagnostik.

SUMMARY

The author recommends the use of a diaphragm of iris-type, in combination with a cylinder, in röntgenological diagnostics, instead of the usual cylinder- and »Loch»-diaphragm.

RÉSUMÉ

L'auteur recommande pour le diagnostic röntgenologique l'usage d'un diaphragme du type à iris, combiné à un cylindre, au lieu du modèle habituel à vanne et à cylindre.

JÄRNHS

Elektriska Aktiebolag

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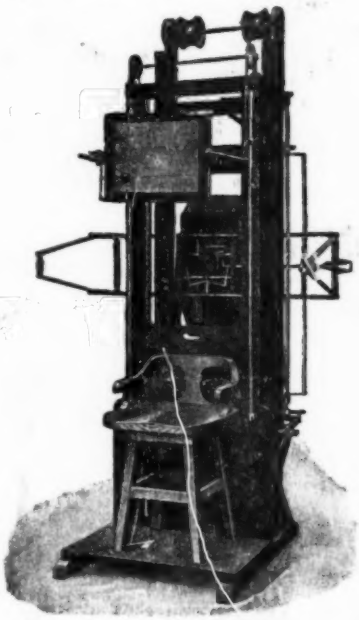

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